MEETING

STATE OF CALIFORNIA

AIR RESOURCES BOARD

SCIENTIFIC REVIEW PANEL

EARL WARREN BUILDING

455 GOLDEN GATE AVENUE

MILTON MARKS CONFERENCE CENTER

AUDITORIUM

SAN FRANCISCO, CALIFORNIA

THURSDAY, DECEMBER 10, 2009

9:39 A.M.

JAMES F. PETERS, CSR, RPR
CERTIFIED SHORTHAND REPORTER
LICENSE NUMBER 10063

APPEARANCES

PANEL MEMBERS

Dr. John Froines, Chairperson

Dr. Paul Blanc

Dr. Craig Byus

Dr. Gary Friedman

Dr. Stanton Glantz

Dr. Katharine Hammond

Dr. Joseph Landolph

REPRESENTING THE AIR RESOURCES BOARD:

Mr. Lyn Baker, Air Pollution Specialist

Mr. Jim Behrmann, Liaison

Mr. Peter Mathews

REPRESENTING THE DEPARTMENT OF PESTICIDE REGULATION

Dr. Marylou Verder-Carlos, Assistant Director

Dr. Terrell A. Barry, Research Scientist III

Dr. Sheryl Beauvais, Staff Toxicologist

Ms. Carolyn M. Lewis, Associate Toxicologist

INDEX

PROCEEDINGS

CHAIRPERSON FROINES: So are we ready?

So we'll bring the meeting to order of the Scientific Review Panel, which is taking up the chemical chloropicrin. And we have a quorum. We're missing one member, Dr. Gary Friedman, but other than that we have a complete Panel.

PANEL MEMBER BLANC: Bearing in mind, that there's an empty seat still.

CHAIRPERSON FROINES: There's an empty position, yes, that hasn't been filled yet.

And so who is going to make the presentation?

DPR ASSISTANT DIRECTOR VERDER-CARLOS: I'll do the opening statement.

CHAIRPERSON FROINES: Pardon me?

DPR ASSISTANT DIRECTOR VERDER-CARLOS: I'll do the opening statements.

CHAIRPERSON FROINES: Oh, okay.

PANEL MEMBER GLANTZ: It's weird to have you down there.

DPR ASSISTANT DIRECTOR VERDER-CARLOS: That's what Dr. Froines said too this morning.

DPR ASSISTANT DIRECTOR VERDER-CARLOS: Good morning, Scientific Review Panel. Good morning, Dr. Froines. And thank you for chairing this session of the

Scientific Review Panel on chloropicrin. I am Dr. Marylou Verder-Carlos from the Department of Pesticide Regulation, Assistant Director for Pesticide Programs Division.

PANEL MEMBER BLANC: Sorry to interrupt for just a second. I'd like the minutes to also show that Dr. Friedman is now with us.

DPR ASSISTANT DIRECTOR VERDER-CARLOS: First of all, thank you to Dr. Paul Blanc and Dr. Kathy Hammond, who spent considerable time with our staff to help improve our draft assessment. And they provided excellent comments on the assessment, which I hope their guidance makes our presentation today clear to all the panel members.

Thanks also to OEHHA staff, Dr. Chuck Salocks and John Budroe, in particular, who joined us to confer the leads last October.

We have also incorporated our responses to OEHHA's final findings in the presentation. However, they were not incorporated in the document in the draft you received from November 10th, but they are incorporated in the presentation. We will incorporate those changes in our next revision of the document.

DPR has had a policy for the last several years of completing risk assessments on all the fumigants. Fumigants by their nature can lead to exposures and

represent about a quarter of the pounds of pesticides applied, and they have varying degrees of hazard.

Our presentation of the chloropicrin assessment today represents our efforts to continue to move forward on our policy to fully assess the risks from fumigants and put appropriate controls in place.

Chloropicrin is currently undergoing a re-evaluation process at DPR. And this risk assessment identified chloropicrin as a probable candidate for a Toxic Air Contaminant. Our scientists will be discussing its use patterns. But typically, it is used as a pre-plant fumigant.

As with all of DPR's risk assessments, we take an approach that incorporates various aspects of risk from our environmental modeling, exposure assessments, and toxicological assessments that consider the maximum rates in the U.S. EPA-approved labels.

There are currently 10 counties that have placed permit conditions on the use of chloropicrin. Those permit conditions mean there can be no applications of chloropicrin unless they are approved by the county ag commissioner.

Since DPR cannot impose restrictions on use by county-based permits without a completed peer review of the risk assessment, we need your external peer review

before we can initiate implementing mitigation measures or regulations.

In the meantime, DPR is currently evaluating end to end statewide permit conditions for chloropicrin, which may be implemented even before the culmination of the TAC process.

Another issue raised about chloropicrin is its use in combination with another fumigant, methyl iodide, which is undergoing application for registration at DPR. And it is currently under review by DPR, and we are working currently with an external peer review committee to review its risk assessment. Methyl iodide is not currently registered for use in California.

At this point, I would like to turn over the presentation to our DPR staff who have prepared the chloropicrin document. Dr. Sheryl Beauvais will present information on exposure assessment. Dr. Terry Barry will present information on the environmental fate. And Dr. Carolyn Lewis will present the health assessment.

Thank you.

(Thereupon an overhead presentation was Presented as follows.)

DR. BEAUVAIS: Hello. I'm Sheryl Beauvais. I'm with the Worker Health and Safety Branch. And if we're ready, I can begin talking.

--o0o--

DR. BEAUVAIS: Chloropicrin, trichloronitromethane -- it's trichloronitromethane -- is a colorless volatile liquid that volatilizes readily in use, and it is strongly and rapidly irritating to eyes and the respiratory system. And that's the key property of it in the risk assessment.

As Dr. Verder-Carlos indicated, it is a fumigant active ingredient in soil fumigation, alone or mixed with other fumigants. And the two that are currently registered are methyl bromide and 1,3-dichloropropene, which is sold under the trade name Telone. You may know it that way.

And there is, of course, a proposed registration of several products with methyl iodide. Those are not registered, and this assessment is dealing with currently registered products. So this is what we'll be talking about today. Although, many of the things that I'm talking about will also apply with the methyl iodide registration if it were to happen, and that's -- that's definitely not a foregone conclusion.

So chloropicrin is a soil fumigant, primarily controls soil fungi and other pathogens and nematodes and weeds.

Another use that chloropicrin has that I'll be

talking about intermixed with this is as a warning agent. And that is it's a -- because it's irritating to eyes, it gets mixed in in low concentrations with methyl bromide, two percent or less, and to -- because methyl bromide has no odor and it's difficult to detect. And so I'll actually talk about what a warning agent is next.

--o0o--

DR. BEAUVAIS: A warning agent is a chemical that has -- such as chloropicrin, it has good warning properties, such as odor or irritation in the case of chloropicrin. Ideally, you want to be able to detect the warning agent at concentrations below which it, and any chemical that it's mixed in with, are toxic.

For soil fumigations, chloropicrin is mixed with methyl bromide at concentrations less than 2 percent. And there are several other products in which chloropicrin is mixed in at higher concentrations with methyl bromide. And in those cases it's considered an active ingredient.

And for structural fumigations, there are two methyl bromide products currently registered that have between 1/2 and 1 percent respectively of chloropicrin, that have instructions for structural fumigation. And then sulfuryl fluoride is the major structural fumigant in California.

And those labels require a co-application of

chloropicrin, in which you pour the chloropicrin into a pan, as you see above here in the upper right-hand-corner. This is a wicking -- what's called a wicking agent in here. It's like a cotton batting, that you pour the chloropicrin in there, place that in front of a fan inside the house, and then that disperses the chloropicrin throughout the house.

So with methyl bromide, when chloropicrin is applied in structural fumigation, it's a mixture, with sulfuryl fluoride, it is not, to just make that clear.

--o0o--

DR. BEAUVAIS: Chloropicrin is in re-evaluation at DPR, because based on data that had been submitted under the California Birth Defects Prevention Act. And we required submission of several new studies from registrants, and we have received all those data and those are incorporated in the assessment.

And what we are here today to talk about is that chloropicrin is also a candidate to be listed as a Toxic Air Contaminant. There will be a full exposure assessment. Is it in preparation right now. It will follow this little more limited assessment by a few months.

CHAIRPERSON FROINES: Does this mean that we're going through the TAC process now --

DR. BEAUVAIS: Yes.

CHAIRPERSON FROINES: -- but that you will be continuing to look at chloropicrin beyond --

DR. BEAUVAIS: Yes.

CHAIRPERSON FROINES -- even beyond what we would --

DR. BEAUVAIS: Yes. The full exposure assessment will contain the occupational and residential, other than what we're talking about today. Today, we're talking about bystanders and people entering homes that have been fumigated with chloropicrin as a warning agent.

And then there are some other scenarios that we'll deal with in the full exposure assessment. But we won't be talking about occupational today, other than occupational bystanders. So people who happen to be picking strawberries, for example, adjacent to an application, we'll talk about those.

CHAIRPERSON FROINES: So we won't take -- this Committee won't take up the work that you do subsequently -- subsequent to this?

DR. BEAUVAIS: I wouldn't expect, no. This is -- we're focusing on the scenarios that are pertinent to its listing as a Toxic Air Contaminant.

PANEL MEMBER HAMMOND: Excuse me. So worker exposures is not relevant to a Toxic Air Contaminant?

DR. BEAUVAIS: Worker bystanders are.

PANEL MEMBER HAMMOND: But not worker exposures?

DR. BEAUVAIS: As far as I know, as in the occupational handlers and so forth.

PANEL MEMBER HAMMOND: That's just done by Cal/OSHA, isn't it?

DR. BEAUVAIS: Well, no, we're doing them, but that's not part of what you're looking at in this document. Basically, in order to expedite the listing of chloropicrin as a Toxic Air Contaminant, we prioritized some scenarios. And that's these. There were a lot of data for occupational, and so it's taking quite a lot longer to get that portion of it done.

PANEL MEMBER HAMMOND: Oh, that's -- oh, okay.

DR. BEAUVAIS: And so in this document, we're looking at screening estimates for bystanders to soil, structural, and enclosed space fumigations; and with the idea that if these estimates are okay, all of the lower concentrations that someone could be exposed to, the full range would be okay as well.

And because of that, when I look at soil fumigation and structure -- or, I'm sorry -- enclosed space fumigation, I'll only be talking about chloropicrin as an active ingredient. Although, it can be used as a warning agent in those settings. It's two percent. It's

a much lower concentration. So the highest exposures are going to happen with the active ingredient use. And then with structural fumigation, because chloropicrin is only used as a warning agent, for those I'll talk about just the 2 percent or less.

--o0o--

DR. BEAUVAIS: U.S. EPA has also been looking at assessing the risk of the soil fumigants, including chloropicrin. Chloropicrin's one of the active ingredients that has risk mitigation measures that are pending and in the process. EPA first proposed them in 2008, and they had amended documents released last May.

They have several soil -- several mitigation measures that were supposed to be coming into effect with the next growing season, followed by buffer zones and some other mitigation measures that are to happen in 2011. So we're running this, you know, just -- this is just sort of background information for you right now. What this assessment deals with is the current product labels and the current regulations. So we're looking at current legal uses.

But EPA is proposing mitigation -- or proposing buffer zones of 25 feet to half a mile. Presently, chloropicrin products -- the hundred percent chloropicrin products do not contain buffer zone requirements, other

than the ones that may be put in place by county ag commissioners, for example. But there are no statewide requirements on chloropicrin for buffer zones.

CHAIRPERSON FROINES: Does that buffer zone of 25 feet to half mile -- how do you take into account meteorology in that process?

DR. BEAUVAIS: Would you like to talk about buffer zones, or shall we hold off on that, or ask Wendy to come up --

CHAIRPERSON FROINES: Your call. Don't let me --

PANEL MEMBER BLANC: Let's come back to that, John.

DR. BEAUVAIS: Okay. And I just want to point out that EPA's risk assessment differs from ours in several ways. And one of them is that they considered -- there's is a re-registration assessment. We are looking at existing products. EPA is looking at products that they would consider eligible for re-registration.

And so, the Chloropicrin Manufacturers Task Force said that they would support certain products, certain uses, and application rates that were different than on existing product labels. And EPA incorporated all of that into their risk assessment.

So they're saying if your products that comply with all of this are eligible for reregistration is the

approach that they take.

PANEL MEMBER HAMMOND: That EPA takes?

DR. BEAUVAIS: That EPA takes. We, however, are dealing with existing product labels and application rates and conditions.

So I'll make that distinction.

--o0o--

DR. BEAUVAIS: And then just to -- here are some of the key differences in the exposure assessment between EPA and DPR. And the first of these is application rates. Current product labels have soil fumigation application rates as high as 500 pounds AI per acre.

And the Chloropicrin Manufacturer's Task Force was supporting a maximum rate of 350. So EPA's risk assessment is using 350. We're using 500. So you see some differences along those lines.

Exposure durations is another key difference. They looked at short-term exposures only. They don't have seasonal, annual, or lifetime exposures, and we do. We'll be talking about those. And the shortest interval that EPA looked at, in terms of calculating exposure, was four hour estimates. So they're looking at four hour peaks. And we're looking at one hour peaks, and we'll be talking about that as well. So essentially, those things factor together to give us higher exposure estimates than EPA.

Also, statistics used to estimate exposure. U.S. EPA tends to go with a geometric mean, as a central tendency estimate of the data. And we're looking at upper bound estimates for short-term exposures and arithmetic means for long-term exposures. And that's the approach that we take.

And finally the --

PANEL MEMBER GLANTZ: How much difference does the arithmetic versus the metric make?

DR. BEAUVAIS: It can be substantial if you've got a skewed data set, and we often do. I don't know about these particular data sets. I can't tell you off the top of my head. But in some data sets, it can be as much as an order of magnitude difference.

And finally, we used ISCST3 modeling in the screening mode as a deterministic approach to generate estimates for bystanders. And Dr. Barry will be talking about that and explaining that.

And U.S. EPA used a probabilistic approach. Now, they did report some of the deterministic estimates, some of the point estimates in an appendix to the risk assessment. But when they talked about the risk estimates themselves, those were all based on probabilistic estimates.

--o0o--

PANEL MEMBER BLANC: I just want to comment that I think it's a very useful summary that you make. And I want to note how encouraging it is to see the pesticide group taking a public health protective approach by choosing an inherently more conservative approach to the data analysis.

And also, I think it is to be commended for using what's actually happening on the ground as your guide rather than some theoretical potential lower level at a future point that hasn't yet occurred.

DR. BEAUVAIS: Thank you.

Currently, there are 47 products registered containing chloropicrin in California. There are -- 25 of those are methyl bromide. And of those 25, seven of them -- I keep wanting to move the arrow, and instead I'm changing the slide. Sorry about that.

Okay, so the second row there that says Chloropicrin WA, that's in blue there, that's the seven products that contain chloropicrin as a warning agent. Those are methyl bromide products, between a quarter and 2 percent. And those are soil, space, and warning agent, and structural fumigation uses. And in all of those again, chloropicrin is considered a warning agent.

There is an individual product that is 10 1/2 percent. And we're not addressing it very strongly in

this exposure assessment, but in the full exposure assessment we actually deal with these scenarios separately. This product was registered with chloropicrin identified as a warning agent even though the concentration is very high.

When we drew that to the attention of U.S. EPA, they weren't aware that the product had been registered. They were surprised to hear that. And I don't know how they're going to deal with that in re-registration. But again, that's very high concentration to be calling a warning agent. So we isolate that one separately.

And then we have 17 products in which chloropicrin is an active ingredient and mixed with methyl bromide. Concentrations of chloropicrin in those products range between 19.8 and 55 percent.

And then as we've mentioned earlier, there are approximately six products, I think, containing methyl iodide that are proposed for registration in California. And chloropicrin concentrations in those products would range between 2 and 75 percent.

CHAIRPERSON FROINES: A question. And this is -- I'm ignorant on this, so excuse me for my question. But the methyl -- obviously, I have a self-interest in methyl iodide at this point.

Going up to 75 percent is not trivial compared to

the numbers that you see above that. Why is 75 percent required with methyl iodide?

DR. BEAUVAIS: That's a good question. I don't know the answer.

One thing I will point out though is that methyl iodide being registered as an active ingredient does not automatically imply that all those products would be registered. Those individual products would be looked at as well. So it may be that methyl iodide, if it were registered, could be registered without that high chloropicrin-containing product. We would look at the products individually as well.

And I don't know the reason for having 75 percent chloropicrin in a methyl iodide product.

CHAIRPERSON FROINES: You realize that from a health standpoint, the obvious -- there's an obvious major question, which is what are the potential interactive effects between Telone and methyl iodide and chloropicrin.

DR. BEAUVAIS: Yeah.

PANEL MEMBER BLANC: Two comments.

One is I would actually correct what Dr. Froines said. I think that -- well, I think what you meant to say is that you have a particular interest in methyl iodide, not that you have a self-interest in it. It could be misinterpreted as implying some kind of conflict of

interest personally, which I know is not what you meant.

CHAIRPERSON FROINES: Did I say that?

PANEL MEMBER BLANC: Yes.

(Laughter.)

PANEL MEMBER BLANC: And then --

CHAIRPERSON FROINES: I always need Paul to keep me on the straight and narrow.

(Laughter.)

PANEL MEMBER BLANC: You know, I notice that this slide corresponds roughly to Table 2 in the document. But in Table 2 in the document, the 10 percent chloropicrin product is not broken out as a separate line.

DR. BEAUVAIS: And I'm sorry about that. I intended to and forgot.

PANEL MEMBER BLANC: So I would suggest that in your final version you did, because I think it is helpful to make that clear.

DR. BEAUVAIS: Yes.

PANEL MEMBER BLANC: I know you have a footnote, yeah. But reading it, it's not as clear as it might be.

DR. BEAUVAIS: Yeah, sorry about that.

PANEL MEMBER BLANC: And the other thing is that, in terms of -- coming back to the question about methyl iodide, which appears on this Table 2, which is good, and with a footnote, is that the only place where explicitly

the issue of methyl iodide is commented on?

DR. BEAUVAIS: Yes.

PANEL MEMBER BLANC: I think it would warrant also a line in the text to make that clearer. And I think that when we come back to talk about the executive summary, I would also suggest -- there's nothing wrong with not devoting effort to methyl iodide in this document, because, you know, it's a theoretical issue at this point.

But I think it should just be more explicit that we will not be dealing with it even -- it's not that we're not aware that were it to be -- because just having it a single footnote in the entire document is probably too obscure.

DR. BEAUVAIS: Okay. It may be in the text too. It's been awhile since I prepared it. I don't remember. But --

PANEL MEMBER BLANC: It's not in the executive summary, I don't think, prominently, not for me to have --

DR. BEAUVAIS: Okay.

PANEL MEMBER BLANC: Just double check on it.

DR. BEAUVAIS: Will do.

CHAIRPERSON FROINES: I should say in my defense that when you chair a committee on methyl iodide and you try and keep everybody working together and everything

going straight, you do actually develop a self-interest.

(Laughter.)

PANEL MEMBER BLANC: Self-protective?

CHAIRPERSON FROINES: Yeah, self-protection.

(Laughter.)

DR. BEAUVAIS: I'll go ahead and wrap up this table here.

And in addition to the products I've already mentioned, chloropicrin is also mixed in with 1,3-dichloropropene in concentration -- in 13 products in concentrations ranging from 15 to 60 percent chloropicrin. All of those are used in soil fumigation only.

And finally, we have nine products in which chloropicrin is the sole active ingredient. And those are for soil, space, and they contain also directions for warning agent and structural fumigation, along with sulfuryl fluoride.

Any more questions about products?

PANEL MEMBER BLANC: Well, just there's an inherent contradiction that you must have struggled with, which is that, in fact, when it's used with Vikane, you're not using 2 percent chloropicrin. You're using a hundred percent chloropicrin.

DR. BEAUVAIS: Right.

PANEL MEMBER BLANC: And so the definition of

it's a warning agent if it's less than 2 percent is a bit challenging. I assume that by weight, if you'd use the weight of the Vikane and then the weight of the chloropicrin that is dispersed in one of those fumigations, does it come out to be -- what percentage of the weight of what's used is chloropicrin?

DR. BEAUVAIS: And I don't know that off the top of my head. I can do that calculation. But I probably should clarify, when I'm saying that 2 percent, I'm really meaning soil fumigation.

PANEL MEMBER BLANC: Right, okay. That would --

DR. BEAUVAIS: And I should just -- in making that clarification would -- but, you're right, I can also check that calculation for structural. And I don't know that at this point.

PANEL MEMBER BLANC: Okay.

--o0o--

DR. BEAUVAIS: So this graph shows chloropicrin use with years across the bottom. And then millions of pounds applied across the Y axis here. And the blue dots there are the total use in pounds applied for all uses. And then because the bulk of the chloropicrin use is in pre-plant fumigation in strawberry fields, I'm showing you the red line here is annual use reported for that.

And in that first bullet up there, I say at least

68 percent of uses were pre-plant strawberry. The reason that I'm making that qualification is that there's a category there of pre-plant soil fumigation, in which crops are not identified.

And so when you look at, for example, that between 2006 and 2007, the total use seems to go up quite a lot more than the strawberry use. And that's -- the difference is due to pre-plant soil fumigation, which the crop is not identified. And a lot of that could very well be strawberries, but I just don't know.

PANEL MEMBER BLANC: Although, I mean, one of the aspects, when I looked at this figure, that I don't think was commented on was strawberries account for the bulk and continue to count for the majority. But, in fact, proportionally, it appears that strawberries are, over time, being less of a proportion. That is to say, there are proportionally more other crops for which it's being used.

And I think that aspect of this was not commented on, because that does have implications for the counties, where it might evolve to be more heavily used in the future. I don't know if it's the same, you know, agri use when you list some of the other crops. So it would be adding maybe one sentence or one phrase in there, you know, of note, however, the proportion over time appears

to be falling -- or the relative contribution of strawberries.

DR. BEAUVAIS: Okay.

--o0o--

DR. BEAUVAIS: And this graph again is we're showing years across the bottom. And we're focusing on acres treated in agricultural applications. And the purpose of this graph is to show -- I've separated out the use reports by products and by concentrations of chloropicrin within the products.

And so the black line that goes with the black diamonds -- or black squares rather, I'm sorry, those are all reported agricultural applications, in which chloropicrin is at least 10 1/2 percent. So it's chloropicrin alone or mixed with methyl bromide or 1,3-D.

And then the white diamonds are chloropicrin in methyl bromide. And these are in -- I'm standardizing in acres treated, because, of course, if I used pounds applied, that would vary quite a bit by the product.

And what this graph shows basically is something that you might predict, as methyl bromide is getting phased out, that the white diamonds there drop down. And the use of methyl bromide in its nearly hundred percent configuration is going down considerably, and chloropicrin is one of the ways -- the hundred percent chloropicrin, or

the higher concentrations of chloropicrin are taking up some of that slack, because you're seeing that you were, you know, approximately 50,000 acres a year.

And basically, as one goes down, the other's going up to some extent. And there are other fumigants that are taking up the slack as well.

--o0o--

PANEL MEMBER BLANC: So that accounts for why the pounds per acre have also gone up essentially, right?

DR. BEAUVAIS: Yeah, that's part of it.

PANEL MEMBER BLANC: That's the explanation --

DR. BEAUVAIS: Yes.

--o0o--

DR. BEAUVAIS: Okay. And this is looking at acres treated per day. Now, I'm going to be -- and when I talk about the exposure estimates, I'll be giving you assumptions that were used in calculating exposure estimates. And so what the purpose of this graph is to help show you how that assumption fits in with what the use data are telling us.

So I'm assuming 40 acres is about the most that someone -- that a crew can treat with a single rate per day in soil fumigation. And so when you look at the Pesticide Use Report, and this is over a five-year period here, how that fits in there is that it's roughly the 80th

to 85th percentile of all uses reported.

And then I've circled in blue up in the upper right-hand corner where they're reporting applications of, you know, 250 acres, or in excess of 150 acres. And what sometimes happens with the PUR is that someone will apply for a series of days and report it on a single day. And so I'm guessing -- certainly that's the case where that's happening, and it may happen in some of the other applications as well. So that's just some uncertainty that's just built into the Pesticide Use Report as we use these data.

And then also I'll draw your attention to the 50th percentile, because for context I'm presenting some estimates also, assuming that if the application size were 15 acres instead of 40, what that does.

--o0o--

DR. BEAUVAIS: And also application rates. And I get those by dividing the acres treated by the pounds applied that are reported in the Pesticide Use Report for individual applications. And I need to note also that application methods are not reported in the Pesticide Use Report. So I can't distinguish between applications through drip irrigation or, you know, which are tarped and which are embedded versus broadcast and so forth.

But across all applications reported -- and these

are applications reported as acres treated, with effectively chloropicrin as a sole active ingredient. And that's -- and the 50th percentile there is somewhere in the range of 111 to 188 pounds AI per acre. I'm assuming in my estimates -- in my screening estimates 500 pounds AI per acre. And as you can see here, that's up above the 99th percentile.

--o0o--

DR. BEAUVAIS: I'm going to change gears now and talk about illness reports coming in for chloropicrin. And so cases are individuals who are reporting exposure or exposure-related symptoms that they believe to be or that there's evidence to support that they've been associated with an exposure to a pesticide. So that's cases. And then episodes are single incidents where a pesticide exposure. And you can have multiple cases in a single episode at times.

So the top graph shows the number of cases again per year. With chloropicrin-only cases are in red. That's a hundred percent chloropicrin products. And the white ones are chloropicrin as an active ingredient, but mixed in with other -- with either methyl bromide or 1,3-D.

And then the blue is chloropicrin as a warning agent. So that would include sulfuryl fluoride

fumigations, structural fumigations of sulfuryl fluoride and methyl bromide, or soil fumigation with methyl bromide.

And so you can see that in 2003 and 2005 and 2006 we've had some episodes with very large numbers of cases associated with them. And those are described in this illness section of this exposure assessment.

PANEL MEMBER BLANC: Just to call to your attention, that there's a formatting error in the draft document, so that these two images are superimposed and that --

DR. BEAUVAIS: Oh, yes. Yeah, that happened when it got converted to the Acrobat, and I'm -- yeah.

PANEL MEMBER BLANC: Just make sure that gets fixed.

DR. BEAUVAIS: Will do.

--o0o--

DR. BEAUVAIS: Okay. And then the most cases in a single episode were a single drift case, 324 cases that happened with a single episode, and that occurred in 2005.

PANEL MEMBER BLANC: So you can have an episode with no cases, is that what --

DR. BEAUVAIS: Well, or --

PANEL MEMBER BLANC: Is that what this means? I mean, so you have cases -- let's take 1992, where you

have -- oh, no, I'm sorry. The scale is different, right?

DR. BEAUVAIS: Yes.

PANEL MEMBER BLANC: Okay.

DR. BEAUVAIS: Yeah, what you're seeing there in 1992, there were no chloropicrin only basically. That's why you're not seeing red bodies there.

PANEL MEMBER BLANC: No, no. It's just that I'm looking at this -- the other axis is different. Here it's your zero five ten --

DR. BEAUVAIS: Yes.

--o0o--

DR. BEAUVAIS: And then we also -- just to look at the types of symptoms reported with these illness cases, this generated this figure for the document. And again we divided this out, chloropicrin alone in the left group of bars, and the center group of bars is a combination again of chloropicrin and either methyl bromide or 1,3-dichloropropene. And then the far right is either sulfuryl fluoride or methyl bromide with chloropicrin as a warning agent.

Red bars are people reporting eye irritation or symptoms related to the eye. Yellow bars are skin. Black bars are respiratory effects.

And then systemic effects, the blue bars are things like nausea, headache and things such as that.

PANEL MEMBER HAMMOND: I recall that the warning agent you were telling us was related to the irritation as distinct from the smell.

DR. BEAUVAIS: Yes.

PANEL MEMBER HAMMOND: But I would have thought eye irritation would always be more than systemic or respiratory, especially when it's as a warning agent. But that doesn't seem to be true.

Do you want to comment on that?

PANEL MEMBER BLANC: Well, it's -- I tell you, I think it's the nature -- this is an -- if you look at the far right series of bars --

PANEL MEMBER HAMMOND: Yes, right.

PANEL MEMBER BLANC: -- those are the symptoms in people who were exposed to a product which was a combination of chloropicrin and Vikane or chloropicrin and methyl bromide.

So with Vikane, you would expect systemic effects. So that's why. And they can't tease out why they were.

PANEL MEMBER HAMMOND: Okay, right. Yeah.

PANEL MEMBER BLANC: What you could say is that it doesn't work very well as a warning agent, since people seem to be exposed to enough of the second part of the product to have non-warning agent effects be more common.

PANEL MEMBER HAMMOND: And, conversely, chloropicrin alone on the left side, it is the large one.

DR. BEAUVAIS: Yes.

PANEL MEMBER BLANC: Now, if you go back to just the previous -- to double figures, two small questions: One, is it the lag time in the DPR analysis of case reports that you don't have 2007 data even?

DR. BEAUVAIS: We do. They're in the process of doing the double checking. They're not publicly available. Nor is that true. That's not true. 2007 are available. That means that figure is old.

PANEL MEMBER BLANC: I would try and update --

DR. BEAUVAIS: Yeah, and in fact the figure in the table -- yeah, that may not be the same as the figure I have in here.

PANEL MEMBER HAMMOND: Yeah, it's actually in the report.

DR. BEAUVAIS: Yeah. So I'm sorry, this may be --

PANEL MEMBER HAMMOND: But we can't read the report because it's overlaid.

PANEL MEMBER BLANC: Right. So then my second --

DR. BEAUVAIS: Okay. Yes. Sorry about that.

PANEL MEMBER HAMMOND: It could be the second one.

DR. BEAUVAIS: Yeah, we do have two --

PANEL MEMBER BLANC: Right, right.

And the other thing, I wonder if someone could simply do for you a regression of pounds of use per year and frequency of illness.

DR. BEAUVAIS: Okay. Well one of -- We are looking at -- and we had talked about this before when we consulted with you about the document about the possibility of doing statistical analysis. And it's straightforward. I've added a little yellow box up here to show that we have in most -- the majority of the cases people are reporting more than one symptom. So that the statistics aren't straightforward for this. We are looking into that, and that is -- yeah. And so probably in a publication rather than in the document itself, because we don't want to hold up the document for that.

PANEL MEMBER BLANC: Fine.

DR. BEAUVAIS: Bet, yes, definitely, that's --

PANEL MEMBER BLANC: It's not a major point, but I think it underscores that it's not just on paper, that there's more pounds used but there's also more illness.

DR. BEAUVAIS: Yeah. Okay.

--o0o--

DR. BEAUVAIS: Okay. Shifting gears again to talk about the environmental fate briefly. And whether

chloropicrin is being used in structural or soil fumigation, it dissipates into the air. That's its major dissipation. It volatilizes out of the soil. And in the -- we have some two-week studies that -- a field of studies that show that on average, following shank fumigation --

PANEL MEMBER GLANTZ: What is shank fumigation?

DR. BEAUVAIS: That's the metal shanks that go into the soil.

PANEL MEMBER GLANTZ: That's what I thought, but I --

DR. BEAUVAIS: Yeah.

Yeah, so, you know, roughly two-thirds of the chloropicrin is volatilized in two weeks -- over a two-week period. And then when you're talking about drip fumigation, that much less of it is volatilized that way, I mean just 15 percent over a two-week period. Or perhaps it's taking longer. I mean two weeks is when they stop monitoring.

Chloropicrin is also degraded both biotically and through abiotic reactions. Field studies show half-lives in the range of one to eight days.

And then once volatilized chloropicrin undergoes a rapid photolysis with half-lives, that's predicted to be less than a day in bright sunlight.

PANEL MEMBER BLANC: Can I ask a technical question that may be -- and in the old days when we had our guy from Riverside, he would answer this. Is there an implication when you use the term "volatilized" as opposed to "vaporized" what you mean? Did you choose that word for a reason?

DR. BEAUVAIS: No, I didn't.

PANEL MEMBER BLANC: John -- John, as a chemist --

CHAIRPERSON FROINES: I'm listening.

Nothing strikes my receptors that suggests that volatilization and -- what word --

PANEL MEMBER HAMMOND: -- vaporized.

CHAIRPERSON FROINES: -- vaporization --

PANEL MEMBER BLANC: I thought when you volatilized something, you heated it up in order to accelerate its --

CHAIRPERSON FROINES: That may be true. I don't know. I've not thought of that, the differences between those two.

DR. BEAUVAIS: There is quite a large literature that talks about volatilized pesticides though as simply --

PANEL MEMBER BLANC: So it's a standard term?

DR. BEAUVAIS: Yeah.

PANEL MEMBER BLANC: Okay.

--o0o--

DR. BEAUVAIS: And persistence in the soil in -- OEHHA actually made reference to that in their finding numbers -- in their findings about environmental fate. And so I'm mentioning that here, that in laboratory soil metabolism studies, the half-life was less than ten days. It tended to be longer in sterile soils, as you predict. But, you know, between 3 and 14 days versus 1 to 4 days again in the laboratory; and again longer anaerobic and in high moisture soils, which would also be sort of anaerobic.

Field dissipation studies reported degradation half-lives between 1 and 8 days.

There's a single report in the literature of soil between a former manufacturing plant in Maine where there were chloropicrin residues as high as 500 milligrams per kilogram seven years after the plant was shut down.

We have no information about, you know, how much was put into the soil and how -- or even how Maine soils compare to California soils. But this does suggest that in some cases you could have residues that persist.

PANEL MEMBER HAMMOND: Isn't there an issue also though that, as you said earlier, that sunlight really enhances the degradation?

DR. BEAUVAIS: Um-hmm.

PANEL MEMBER HAMMOND: And I would imagine different layers of the soil are really -- would actually have different half-lives.

DR. BEAUVAIS: Yeah. That makes sense, yes.

Yeah, that's a good point, that the --

CHAIRPERSON FROINES: Do you know that -- the timeframe for the study that studies that reported degradation half-life being 1 and 8 days, do you know what -- how long they went?

In other words, were they eight days?

DR. BEAUVAIS: I don't know if those are -- the studies are summarized in the document. I don't know if --

CHAIRPERSON FROINES: Yeah, okay.

DR. BEAUVAIS: Yeah.

PANEL MEMBER LANDOLPH: You don't have to change the slide. But I just had a quick question about the previous slide on the illnesses, where you mentioned that most of them were eye irritation, skin and systematic symptoms. Were there any pulmonary symptoms that were permanent and not reversible, any edema-like changes or --

DR. BEAUVAIS: I don't know.

PANEL MEMBER LANDOLPH: Okay. Thank you.

CHAIRPERSON FROINES: Well, Joe, that's an

important question. Because as we know from the methyl iodide, the case studies show very, very long chronic defects that were really quite devastating over a long period of time. And so the question becomes, what's the -- are there very longstanding effects?

PANEL MEMBER BLANC: Well, I think we should return to this when we come to the Health Effects section, because this is really a different --

CHAIRPERSON FROINES: That's why I was -- I was waiting.

PANEL MEMBER BLANC: But on the Maine -- the case report from Maine of the factory which OEHHA brought up in their response. And I saw that the papers were cited in this document. But insofar as they touched on the laboratory analysis of the soil, can you point out where in the document you also summarized this thing about the people -- the illness and the soil samples and all of that in the factory in Maine?

DR. BEAUVAIS: Okay. I didn't summarize anything about illnesses with the factory in Maine. I just pointed out as part of the environmental fate that there was the single report.

PANEL MEMBER BLANC: And where is that?

DR. BEAUVAIS: It should be in Soil -- Persistence in Soil section.

PANEL MEMBER GLANTZ: It is. And I don't remember where it does, but I remember reading it.

PANEL MEMBER BLANC: Okay. I read it in the OEHHA and then I went back to try to find how you'd handled it in the document. And I saw -- you don't have to -- I mean just tell me later, just confirm to me later that you were able to find it.

DR. BEAUVAIS: Okay.

CHAIRPERSON FROINES: Are you suggesting that if it's not there, that she put something in?

PANEL MEMBER BLANC: Well, yeah, I thought it -- since OEHHA brought it up specifically it terms of that. But what we can do is come back to the -- when we get to the Health section, let's see if that case report made it to the health part.

DR. BEAUVAIS: Okay.

PANEL MEMBER BLANC: Because the OEHHA -- or we can clarify it with the OEHHA people. But they specifically talked about symptomatic people prompting the sampling and so forth.

DR. BEAUVAIS: Okay. One comment I also wanted to make in response to Dr. Landolph's question about illnesses, and just to note that in general the way that the illness reporting system works is that we may not be aware of long-term illnesses, then just to complete that

question.

PANEL MEMBER HAMMOND: I think this is important. That's a good point and that's very important.

CHAIRPERSON FROINES: That's a very important point.

--o0o--

DR. BEAUVAIS: Okay. And then also this is another part of the finding that OEHHA had raised. And, that is, the question of whether it could persist in groundwater and perhaps travel a distance. And so here's the information that we have about groundwater contamination.

First of all, chloropicrin is on DPR's list of pesticides that could potentially contaminate groundwater. It's there because of its physical -- chemical physical properties. It's highly water soluble and doesn't absorb the soil very much, and fairly lengthy hydrolysis according to the wind environmental monitoring folks who are looking at this.

However, between 1986 and 2003 there were a total of 1700 well water samples collected in 34 California counties with no detection of chloropicrin.

So that's the information that we have out there. That's not to say that question has certainly -- has been answered, but this is what we know about it.

PANEL MEMBER HAMMOND: And of those 1700 wells, how many of them were in the counties? Are these all in the counties that actually use chloropicrin, or are they just wells in the state.

DR. BEAUVAIS: They'd be wells in the state. And so it's quite -- it's a range of counties it would include.

PANEL MEMBER HAMMOND: So might it be to at least make sure that some of the warmer states -- the counties were used.

DR. BEAUVAIS: Yeah, as in -- you know, in Monterey and in Kern, you know, absolutely, yes. And actually, yeah, and I have looked enough to know that.

PANEL MEMBER HAMMOND: That's good to know.

CHAIRPERSON FROINES: Well, I missed -- I'm sorry, I missed that.

PANEL MEMBER BLANC: That these wells include some wells --

PANEL MEMBER HAMMOND: Well, because they've been used in ten counties -- ten counties, is it?

DR. BEAUVAIS: Thirty-four counties.

PANEL MEMBER HAMMOND: Thirty-four counties in the state.

DR. BEAUVAIS: Yeah, with the counties where chloropicrin is used.

PANEL MEMBER HAMMOND: Chloropicrin is used in how many counties?

DR. BEAUVAIS: Oh --

PANEL MEMBER HAMMOND: I thought it was only ten counties. Am I wrong?

DR. BEAUVAIS: I don't know.

PANEL MEMBER BLANC: The bulk is used in --

PANEL MEMBER HAMMOND: Most of it's used in ten counties?

DR. BEAUVAIS: Yeah, it's more than ten counties, yes.

PANEL MEMBER HAMMOND: And so I just wanted to make, you know --

DR. BEAUVAIS: There is an overlap, yes.

CHAIRPERSON FROINES: But the other question that goes with that is, when the samples were collected in the 34 counties, what's the relationship between the use of chloropicrin in those counties and the actual study itself? Because obviously if you're not using chloropicrin, you may not find something.

DR. BEAUVAIS: Yeah. Well, and of course it's an issue where again our pesticide use reporting data are very helpful, but they only go down to a one square mile resolution.

PANEL MEMBER HAMMOND: But even if you got

that --

DR. BEAUVAIS: Yeah.

PANEL MEMBER HAMMOND: -- it would be useful.

Yeah, it might be worthwhile to see of those reports which of them would you have predicted might have had some.

DR. BEAUVAIS: Okay.

Okay. Anymore questions about that? Because I'm moving on to talk about how exposure was calculated.

--o0o--

DR. BEAUVAIS: Okay. So I'm presenting estimates for short-term durations, of 1 hour, 8 hours, and 24 hours. These are all upper bound estimates because we want a realistic worst case for these. One hour because chloropicrin-associated irritation occurs rapidly. We look at 8 hours because of occupational bystanders. And then 24 hours for residential bystanders.

And then for seasonal, annual, and lifetime exposures, because in some agricultural areas we would expect repeated exposures could potentially occur for multiple fumigations if you live in an area where there are a lot of strawberries grown, for example.

And in those cases we want typical exposures, because of the longer intervals we wouldn't expect that people would consistently have high-end exposures,

particularly when you look at, you know, how they -- the way that the use reports are, you have a lot of small applications happening.

PANEL MEMBER GLANTZ: One thing that wasn't clear to me when I read the report, when you're looking at the lifetime exposures, are you assuming that the person spends their whole life living in the same place?

DR. BEAUVAIS: Yeah. Or in same conditions anyway, yeah.

PANEL MEMBER GLANTZ: Okay.

--o0o--

DR. BEAUVAIS: So we have soil fumigation air monitoring data provided by the California Air Resources Board. And they did both ambient air and application site monitoring. And those are all summarized in the document.

And then also we have Chloropicrin Manufacturers Task Force data for soil fumigation. And these are from the registrants. And those concentrations associated with that monitoring turned out to be higher, and so for bystander estimates are based on the registrant data.

PANEL MEMBER HAMMOND: That's new in the November compared to the May document.

DR. BEAUVAIS: No, that's going to be structural fumigation that's changed.

PANEL MEMBER HAMMOND: Oh, I'm sorry. So that's

not --

DR. BEAUVAIS: This is the same.

PANEL MEMBER HAMMOND: Okay.

DR. BEAUVAIS: And so for when the registrants did their monitoring, they used both on-site and off-site measurements. And we used on-site measurements, and I'll be describing those here in a second. And those were what were used to estimate exposure.

And we have two sets of studies conducted by the registrants: First was conducted in the mid-nineties in Arizona, Florida, and Washington. And then we have a more recent data in response to DPR requests that were conducted -- studies conducted in California 2003 and 2004.

--o0o--

DR. BEAUVAIS: They were all conducted the way that these studies tend to be conducted for chloropicrin, which is using the XAD-4 resin in the air samplers, with the backup sorbent sections. And so we have a sense of whether there is any sort of breakthrough happening.

CHAIRPERSON FROINES: Can I ask you a question?

DR. BEAUVAIS: Sure.

CHAIRPERSON FROINES: Go back to the last slide.

ARB did the top monitoring?

DR. BEAUVAIS: Yes.

CHAIRPERSON FROINES: -- of the ambient air monitoring?

DR. BEAUVAIS: Yes.

CHAIRPERSON FROINES: And the Chloropicrin Manufacturers Task Force did the second one. And what I wanted to ask ARB was, did you have any data that was not ambient monitoring?

DR. BEAUVAIS: They did. I can actually answer that question.

CHAIRPERSON FROINES: Oh, okay.

DR. BEAUVAIS: They did. And that's summarized in their as well. If they had applications, they did monitoring associated with the applications, yes.

CHAIRPERSON FROINES: Did the application site monitoring?

DR. BEAUVAIS: Yes, they did. For several actually multiple applications.

CHAIRPERSON FROINES: So you can compare the results from ARB with the results from the manufacturers?

DR. BEAUVAIS: Well, their estimates tended to be lower.

CHAIRPERSON FROINES: Whose?

DR. BEAUVAIS: ARB's. Yeah, I'm using -- I'm actually using the registrant data because they were higher.

--o0o--

DR. BEAUVAIS: And so sampling locations. And I talked again -- and I also want to emphasize that the field sizes in these studies were between five and eight acres. So those are smaller than what we need for our exposure estimates.

So on-site in this -- this square here represents a field. And the little numbered circles that run off it represent off-site samplers at a series of distances.

And I also wish to note that none of those are at the edge of field. And yet because we don't have buffer zones for chloropicrin, bystanders could really be at their edge of the field in some cases. And so we needed to be able to estimate exposures there.

Secondly, on-site samplers are in the center of the field. You have an on-site sampling mast that -- and I'll show that -- I have a slide here to show that in a minute.

--o0o--

DR. BEAUVAIS: Yeah, these are what the on-site samplers look at. So it's a sampling mast with a series of samplers on it at the center of the field. And they look -- and from that, you can get changes in concentration of air of chloropicrin and changes in temperature, wind speed. And these changes with height

are then used to calculate the flux of chloropicrin from the soil surface, where flux is the amount of chemical emitted per unit area in time. And that can then be used to calculate off-site concentrations. And we do that for -- as I noted, we need to be able to get to concentrations for applications that are larger than the ones that were monitored and for people that are closer than the samplers were and under different weather conditions.

--o0o--

DR. BEAUVAIS: And so at this point I'm going to turn this over to Dr. Barry, and she's going to describe how she did this -- what she did and how.

DR. BARRY: Good morning. I think I might need the arrows since I don't have a pointer.

DR. BEAUVAIS: Haven't figured out how to do that without turning the slide.

DR. BARRY: Oh. Well, okay, I'll be careful then.

Okay. So actually the question about comparing the ARB and the chloropicrin task force data could be addressed as I start with this.

One of the things we're going to talk about is the fact that we used air dispersion modeling to produce our estimates, our air concentration estimates for the

exposure appraisal.

The best way to compare studies is by having flux estimates from the different applications and the different studies. For the ARB studies, there wasn't enough data to calculate flux. So it's difficult to calculate just straight air concentrations like that have measured just off-site. You need actual volatility to be able to compare the different methods and the different sites and things like that.

So that's why we concentrate on the chloropicrin task force data, is because it's going to allow us to have a flux estimate.

Okay. So we used air dispersion modeling to estimate those air concentrations that are used later in the exposure appraisal. And air dispersion models use the emission information from one or more sources to estimate chemical air concentrations. We use specifically a Gaussian plume model. And Gaussian plume models have inputs of:

Field volatility, which we've talked a little bit about. It's often called the flux.

The dimensions of the source, the orientation of the treated field, the distance from the field that the receptors are interested in are, and whether you've got urban or rural dispersion patterns. And in our case,

we're using rural dispersion patterns because we're in agricultural areas. And that does produce higher air concentrations. There's not as much vertical mixing with rural dispersion.

They also use meteorological inputs, temperature, wind speed, and atmospheric stability.

And we're using the Gaussian plume model in what's called screening mode, as Sheryl mentioned. And in that case, the model is used to predict reasonable worst-case ground level or breathing air concentrations that may occur off-site by examining the full range of meteorological conditions across all stability classes and wind speeds that might occur. And then we settle on the set of conditions that generate a worst-case -- reasonable worst case air concentration.

--o0o--

DR. BARRY: Okay. So to give you an idea of the Gaussian plume form, this is a bird's-eye view of modeling that was done actually on one of those incidents that we talked about earlier on the illness slide. This was in Mettler, California, in 2003.

And this shows how a plume will originate from a source. And the source is the rectangle that's sort of in the center of those isopleths. The bottom quarter rectangle or half rectangle of that area was applied. And

the plume will move away from the field as it's affected by wind speed and direction, and the volatility of the material of course.

Well, this incident occurred over two nights. This is the first night. That represents about 18 acres there that you see in the field. And the wind direction is moving from east to west. And it's narrow because it's going along the long access of the source. So you can see that the plume dimension crosswise is affected by the dimensions of the source also.

And these isopleths represent your typical Gaussian form.

PANEL MEMBER GLANTZ: What are the numbers?

DR. BARRY: Oh, I'm sorry. Those are -- that's ppb.

PANEL MEMBER GLANTZ: And then are the red dots and the blue dots anything in particular?

DR. BARRY: Yes. The blue dots are an apartment complex that was affected the first night. Most of that complex I believe was evacuated and people had eye irritation and things like that.

And you can see that the model is predicting under those meteorological conditions, which were highly stable and low wind speed. It was just after sunset. We're talking 150 to 200 ppb, 100 ppb, right about in the

range of where people's eye irritation would be expected to occur.

And then the red -- the next slide you'll see what happens to the red dots.

--o0o--

DR. BARRY: Okay. So this is the second night. They continued to apply the -- they thought that, you know, things were dealt with. And then the second half of the field at the top was applied.

So now you've got the first rectangle was day one, and then at the top is of that -- let's see, can I do this without changing the slide? Where's the arrow?

Okay. I can't do it.

Okay. You've got a square area. The top of the square is applied the second day.

So now, this is the second night. Again, it happened just after sunset, low wind speeds, and stable atmospheric conditions. And the red dots on the bottom there -- I'm not sure what the yellow one is. I'm sorry. But the red dots are households that were evacuated and affected. Same symptoms.

And the thing to note on here is that now you see that the plume is wider, you know, the air kind of -- that's about a half mile. Both directions are about a half mile. But the plume characteristic has changed

because the dimensions of the field have changed.

The met conditions are pretty much the same.

We've also got some changing in the flux. The flux will be lower on the first half of the source than the second half because the first half was applied the night before.

PANEL MEMBER HAMMOND: Could you go back a slide please?

DR. BARRY: Sure.

PANEL MEMBER HAMMOND: So your estimates are that the concentrations that first night are around 250.

DR. BARRY: Yeah, be 200 -- 200, 250. Well, right in the neighborhood is -- yeah 200, 250, uh-huh.

PANEL MEMBER HAMMOND: And then going forward, they're really about the same --

DR. BARRY: About the same, uh-huh.

PANEL MEMBER HAMMOND: -- about 200, within the -- the estimates are about the same.

DR. BARRY: And same symptoms, eye irritation, you know, things like that. I mean there's a range of symptoms. And actually we have a peer-reviewed general article that covers this incident in Journal of Agri-medicine, I believe is what it is.

I mean the case -- the case reports are all reviewed in that Journal article.

PANEL MEMBER GLANTZ: How long after application was this?

DR. BARRY: Several hours. You know, you apply it during the day. And if it's occurred -- they tend to occur either early in the morning or at sunset, because that's when you get stable atmospheric conditions and low wind speed. And a little bit of flux goes a long way under those conditions, a little bit of material.

Okay. So you also saw the change in wind direction.

So the first night nothing happened to the neighborhood on the bottom, you know, second night nothing happened in the neighborhood to the west.

--o0o--

DR. BARRY: All right. So DPR uses the ISCST3 model. This is an EPA Gaussian plume model.

The features of the ISC model are that, first of all, it's considered to be steady state or it's assumed -- it has to be steady state, which means the conditions of the meteorological variables do not change within an hour -- or are assumed to not change. So if you have a wind speed of one meter per second, you assume it's one meter per second for the entire hour, that you're not getting variations during that hour.

The Gaussian plume form, the chemical

concentrations are highest at the center and then they taper into a bell-shaped curve, both crosswind and in a vertical profile. So you can see -- and I'm sorry I don't have a pointer. But the crosswind and the vertical direction are both bell shaped.

And then we use the air concentrations that are along the plume center line, which are the highest.

Now, this figure shows that it's a point source. But the same futures hold for area sources, and we used area sources to represent our agricultural fields.

A suggestion has been made that we should change from ISC to what's called Air Mod, which is a next-generation Gaussian plume model, instead of using ISC for our modeling. But the improvements in Air Mod only really apply to a point source, which is like a smoke stack's there. And for soil fumigants we're using area sources. So there's no difference between using those two models. So we've elected to stay with ISC at this point.

PANEL MEMBER BYUS: I have just a question.

DR. BARRY: Yes.

PANEL MEMBER BYUS: So you're saying it's a point source of -- you're saying it must be a point source up off the ground then to get that vertical component, the largest concentration --

DR. BARRY: Yes.

PANEL MEMBER BYUS: -- up off the ground?
DR. BARRY: Yeah, it --
PANEL MEMBER BYUS: But that isn't what happens, is it? I mean in a sense isn't it a -- I mean doesn't it leak from the ground level up?
DR. BARRY: That's a very good question. And what happens with a ground source is -- where is it? Am I doing this wrong?
Oh, okay. Sorry.
With a ground source you're basically getting -- you're getting half, you're getting -- how the model -- and that's a very good question. How the model operates is it's a virtual reflection basically.
PANEL MEMBER BYUS: All right. That's cool.
DR. BARRY: Yes. But it is a Gaussian form. It's just cut in half if it's originating from the ground.
Yeah, very good.
PANEL MEMBER BLANC: And then, just in -- you're talking about your choice of models. But this doesn't touch on the perfume yet, but you're going to get to that --
DR. BARRY: That's a good question too, and I'll -- I'll address that when I get to the screening mode aspect, because that actually goes to that question.
PANEL MEMBER BLANC: Okay.

DR. BARRY: Yeah. Good. Thank you.

So we're ready to move on?

--o0o--

DR. BARRY: Okay. So as I said, we're using the ISCST3 model. This is the primary model that's been used by DPR since 1992. We used it to develop all of our methyl bromide buffer zones and other mitigation measures that we developed. It was -- we were put through a National Academy of Sciences peer review on that.

I did mention that we had a peer-reviewed article on that incident. We've also got -- we've got five articles actually that have been published using ISC and screening mode methods on covering metam sodium and chloropicrin incidents. And they've been published in public health and toxicology journals.

Now, what I've shown here is a simplified form of the model, just so that we can get down to the fact that this model is really two main parts. The first part is the F value here, which is flux or the volatilization. And then the second part is the more complicated function that includes meteorology and also where you are in respect to the source. So how far downwind are you? How far off the center line are you? How high off the ground are you? And those two things together get multiplied to produce the air concentration.

So all other things held constant. So if this M is held constant, air concentrations are directly proportional to the flux, which makes it very convenient for comparisons of different application methods and mitigation measures and things like that.

--o0o--

DR. BARRY: Okay. So we are using screening methods. Sheryl mentioned that. And we use this to produce reasonable worst-case air concentration estimates.

The U.S. EPA guidelines for screening analysis does state that there is a relatively large degree of conservatism that's incorporated into a screening procedure. And we use that to provide reasonable assurance that we are getting maximum concentrations so they will not be underestimated. And that's the real reason that we've chosen screening methods at this point.

When we use screening methods, the averaging time of the air concentration that's produced is directly related to the averaging time it produced the flux. So, for example, you'll see later that for chloropicrin, most of the task force sampling air was with six hours. So our air concentration estimate's going to be a six-hour estimate in that case.

The meteorological data in screening mode is considered to be a predominant condition for that

averaging time. The thing to really understand is that even though these are screening method -- screening meteorological conditions, they can and do occur in the environment. And in fact, our one-hour screening met condition is one meter per second in F stability. Well, one meter per second in F stability is what was the conditions on that incident that I showed you, that figure that I showed you. So it does occur.

The other --

PANEL MEMBER GLANTZ: Can I ask a dumb question.

What -- could you just briefly describe what screening mode is and what the alternative to screening mode was?

DR. BARRY: Screening mode means that we're looking at worst case. So in other words, when you're doing air modeling, you're going to get the highest air concentrations for a given flux under very stable and low wind conditions if you're doing a ground level source.

So we are only looking at that condition. We're not generating a distribution. And in effect, I'll talk about perfume in a moment and the probabilistic model.

PANEL MEMBER GLANTZ: Talk about what?

DR. BARRY: The perfume model, which is a probabilistic model. Because that is -- you're asking a very good question actually that we've had discussions

about.

So let me cover the wind direction. And then I've got --

PANEL MEMBER GLANTZ: No, that's fine.

DR. BARRY: Yeah, and then I've got a discussion about -- I'm going to actually talk about exactly what you're asking.

PANEL MEMBER GLANTZ: Okay. Well, I'm glad it was a good question.

(Laughter.)

DR. BARRY: Well, the thing is is that it's also --

PANEL MEMBER BYUS: I still think it was dumb.

(Laughter.)

DR. BARRY: It's also related to the wind direction question. So when we're doing screening, the wind direction is interpreted as a predominant direction of an averaging time.

And this also gets to your question. Because one of the criticisms we've had of our 24-hour screening condition is that the wind direction can't possibly go one direction for 24 hours. That's not what we're assuming. What we're assuming is, and what is really embedded in that screening 24-hour mode, we're seeing 24-hour flux. That's what I said, the averaging time is relative to the

averaging time of the flux. So if it's 24-hour flux, you've got incorporated in there all those variations that occurred in the measurements over 24 hours.

When you use that wind direction and that wind speed, what you're assuming is you've averaged the meteorological condition over that period too. So if it's 270 degrees, it means on average for 24 hours it's going to go to 270 degrees.

So now, that's screening. So you're only using the highest flux and what you consider to be the worst conditions.

The other method which is the perfume model, which you might have seen in some of the comments that were associated with our modeling, it uses the ISCST model. It's the same model produced the air concentrations. But what happens is it uses five years of weather data to produce distributions of air concentrations. And then you have to make a cut of what percentile do I want.

Well, we're basically at the upper percentile. We have chosen in advance that we're going to only -- that we're looking at, you know, 99.9 or whatever, the upper bound.

Although, for the one hour, one meter per second in estimability occurs very frequently in the environment.

So we're talking -- we're not just talking about one point at the top of the percentile. We're talking about that little straight line that occurs right at the top, you know, if you line up all your weather conditions.

So, at this point we're interested in estimating that reasonable worst case. The Department has chosen to do that, and that's why we're going with this.

But at some point later, you know, we may have examined that probabilistic method. And that's the alternative is using the probabilistic method.

PANEL MEMBER BLANC: And then how does that apply when you start to get to the seasonal and the lifetime? Because then it seems that a probabilistic meteorologic calculation might make more sense or -- because you don't have lifetime flux data. You're extrapolating out from the flux data that you have.

DR. BARRY: We have a model that we've looked at in-house called SOFEA that can produce -- what you end up doing is producing, say, 70 years of agricultural applications, then looking at concentrations, and in trying to estimate chronic exposures. And that would be something that may be looked at in the future for chloropicrin.

But right now the way we're dealing with that is with the peak-to-mean adjustments that I'll talk about in

a little bit. Because you can -- you can -- I actually don't want to get ahead of myself on that. I've got a slide on it.

PANEL MEMBER BLANC: We'll wait.

DR. BARRY: But we are doing a screening mode on that too. It is a possibility to do that without using probabilistic methods.

PANEL MEMBER BLANC: I see.

DR. BARRY: But there are positive features to use in the probabilistic method certainly also. At this point we're just still doing the screening method.

So let me get to those slides, and I think it will make more sense.

--o0o--

DR. BARRY: Okay. So to estimate a reasonable worst case air concentrations, we need to have a flux, because that's one of the main inputs in the model. So, in order to get that, we have flux profiles that are generated from field studies. And we mentioned we're only using Chloropicrin Manufacturer Task Force studies to look at the exposure appraisal concentrations. And the reason is we have what are called direct flux estimates from these studies. What that means is there's a center mass in the field. Sheryl showed you that picture. And it allows you to actually measure the rate at which the

chloropicrin is coming off the field. And then you can put that into the model -- the ISC model.

This graph shows a flux profile. So, for example, during the application period the chloropicrin is coming off of that six-hour period at approximately 40 micrograms per meter squared per second for six hours. So you can calculate a mass from that too.

And then here you've got the sampling interval after the application was finished - 180 micrograms per meter squared per second. And then so on.

And this is the first 60 hours or so of the application. All of these are equal interval. They're all six hours.

You don't have to have equal sampling intervals. It's just the case in this particular study.

PANEL MEMBER BYUS: So I have another dumb question.

So then the flux goes up because it's diffusing closer to the soil? Why is the flux increasing?

DR. BARRY: That's a good question.

(Laughter.)

PANEL MEMBER BYUS: That's why I'm asking it.

CHAIRPERSON FROINES: I'm glad you -- the DPR folks keep telling us that our questions are good. I would rather not get sued again for questions that are

dumb.

DR. BARRY: It's actually the $64,000 question.

(Laughter.)

DR. BARRY: There is a lot of research that has gone on to try to quantify exactly what causes a flux to go up and, as you see there, that peak or why it bounces around the way it does in this figure or why -- I'll show the next slide where there's multiple field studies and the flux profiles all look a little different.

There are a number of different factors. It could be the soil type, the temperature, the depths of injection, the meteorological conditions, the tarp or no tarp.

But what is fortuitous for us is with methyl bromide we have a very large database on flux estimates, and application methods tend to be reasonably similar in their flux profile. So we don't -- we haven't done the research in separating all the different factors. And we don't really have a model yet that will like model how flux will change if you change the depth or whatever. That's coming.

But there are a whole host of factors that could affect the flux. But we do see the same patterns over and over again. For example, this peak is not unusual. That occurs across fumigants with an untarped application. You

put it in the ground, it tends to come out rapidly. If there's a tarp, it might be stopped -- you know, slowed a little bit. With drip irrigations there tends to be a peak right after they flush the lines. So, you know -- and it's consistent across fumigants.

But there's a lot of research going on to answer that question.

PANEL MEMBER GLANTZ: Well, could it also be related to the time of day that you did the application?

DR. BARRY: Yes.

PANEL MEMBER GLANTZ: Because the day -- if you applied it in the morning and then it warms up, that could maybe account for the peak.

PANEL MEMBER BLANC: Well, there are -- I mean just to clarify, at hour 4 they're still in the process of applying. So this isn't time -- this time doesn't start at the completion of the application. So if they have a ten-hour application, this is really -- that peak is at the point at which they've finished applying.

PANEL MEMBER GLANTZ: Oh, okay.

PANEL MEMBER HAMMOND: It's almost --

PANEL MEMBER BYUS: Hours post-application.

DR. BARRY: Yeah, these are the midpoint. So this is the midpoint -- this is the midpoint of the interval -- time zero is the beginning of the application.

So this does include --

PANEL MEMBER HAMMOND: So it's really the hours since the start of application.

DR. BARRY: Well, yeah.

PANEL MEMBER HAMMOND: Well, I mean it's an important difference.

DR. BARRY: This is zero. This is the beginning --

PANEL MEMBER HAMMOND: Zero means the beginning --

DR. BARRY: -- the beginning of the application. So this includes the application period, yes.

PANEL MEMBER HAMMOND: And the application goes for eight hours?

DR. BARRY: No. It was about --

PANEL MEMBER HAMMOND: Well, a particular one --

DR. BARRY: It was only a couple of hours. And this is a six-hour interval. So there's like a little -- a short period of time after the application that this is still being sampled.

PANEL MEMBER HAMMOND: That sample started at zero?

DR. BARRY: Yes.

PANEL MEMBER HAMMOND: -- time zero?

DR. BARRY: This captured the entire application.

And that is -- with the field studies --

PANEL MEMBER HAMMOND: Did it stop when the application stopped?

DR. BARRY: Yes.

PANEL MEMBER HAMMOND: The application went for six hours?

DR. BARRY: Well, yeah, give or take, yes. Within minutes, yes.

PANEL MEMBER BLANC: So does this figure appear in the document as such?

DR. BARRY: No, I believe it's in my -- only in my memos.

PANEL MEMBER BLANC: Okay. Because I would say if it's in the document, you should change the label there to clarify.

DR. BARRY: Okay.

PANEL MEMBER BLANC: I mean I would look at it in -- I mean maybe it's over-simplistic, but I kind of look at it if you'd measured when is the highest exposure at the side of your automobile to gasoline as you filled the tank? Probably the flux increases as you get closer to, you know, the filling of the tank. And I think with this too probably is they put more and more stuff in the soil. At first there's very little, it's fluxing off. And then it --

PANEL MEMBER HAMMOND: I think the analogy's not a good one. I think it's a poor analogy. But it does make sense to me -- it does make sense to me that what we're seeing is, given that the application is happening during the graph there --

DR. BARRY: Yes.

PANEL MEMBER HAMMOND: -- is that there's more surface area that has gotten more material there.

PANEL MEMBER BYUS: Yeah, that makes more sense to me.

PANEL MEMBER HAMMOND: But it's the volatile part of the tank that matters, not the liquid.

DR. BARRY: The peak does tend to occur after the application's finished, depending on the application method. I think only sprinkler metam sodium is the peak during the application. Usually it's delayed. Usually it's delayed by several hours.

PANEL MEMBER HAMMOND: I wonder if there are things that happen, things one does at the end of an application that would encourage that. I don't know.

DR. BARRY: Yeah. Again, you know, we're looking at modeling flux, but it's not an easy question.

PANEL MEMBER BLANC: Okay.

DR. BARRY: We are in the process of doing that though, I will tell you that.

PANEL MEMBER BYUS: Intuitively it was like -- I would -- it was a concentration gradient. So the concentration is constantly falling. So you would predict the flux -- I mean without thinking about how it was applied and how it's coming forward. I mean that's why I asked the question.

--o0o--

DR. BARRY: DR. BARRY: Okay. Well, this little peak here, for example -- where is this? I'm having trouble finding this dot. It must be my eyesight.

Anyway, the second little peak there is -- you do see that kind of pattern sometimes with the fumigants. It depends on the application method. But you will see that pattern.

PANEL MEMBER HAMMOND: But this is experimental data, not model data, right?

DR. BARRY: This is measured data, yes.

PANEL MEMBER HAMMOND: Yeah. So I mean this could relate to some heat, you know, that the air temperature just heats the soil and so more is given off.

DR. BARRY: Oh, yeah, yeah. Or it could be at night. With metam the highest flux occurs at night.

PANEL MEMBER HAMMOND: But, again --

DR. BARRY: Yeah, I know. I got the graphs to show you it does occur.

--o0o--

DR. BARRY: Okay. So that was one flux study, and that is -- okay. Could you tell me where the red dot is? Why am I not seeing this?

Okay. Well, I'll just -- I'm going to have to use this.

The upper left-hand graph is the one I just showed you. I have to explain the axes here, because just the way this software produces this axis, it doesn't label on the sides and bottoms.

The side -- the Y is flux and the X is hours. And it's hours -- zero is the beginning of the application. Okay.

So I have normalized all four of these to the maximum application rate that's allowed on the label, as Sheryl -- and what Sheryl used in her exposure appraisal. So they all -- you can look across graphs. That on top is a little bit difficult because it has half the allowed application rate. But you can look across and see how the flux profiles vary.

And these are different methods, and that's why.

And a broadcast/untarp method produced the highest six-hour and highest one-hour flux estimates in the air concentrations. And you can see that that would be the case because of that high point there.

The bed/tarp, which is the lower left-hand, produced the highest 24-hour flux and the highest 24-hour air concentration. The reason is you're averaging four of those dots, because those are six-hour averages at that point. Starts out six hour and then goes to 12 hour, which is why they get closer together.

PANEL MEMBER GLANTZ: So is the tarp put down and then it's injected through the tarp?

No, it's injected --

Or do they inject it and then put the tarp down?

DR. BARRY: Yeah, the tarp gets rolled as they're injecting, behind it.

PANEL MEMBER GLANTZ: What's the difference between broadcast and bed?

DR. BARRY: The beds are formed -- either pre-formed or they're formed as you go. And they can be 36 inches or so or more wide. And then there's a furrow in between, and the furrow is not tarped.

PANEL MEMBER GLANTZ: Okay.

DR. BARRY: And we see the same pattern with methyl bromide, where the bed tarp tends to look just like this because it comes out either -- in the furrows. Or another possibility is that the tarp is stretched and it comes out the tarp differently, that the permeability is changed. So the broadcast is just flat.

PANEL MEMBER BLANC: Then does the broadcast have the largest area under the curve altogether?

DR. BARRY: I can tell that you actually.

Okay. The mass loss, because that would be -- you can integrate -- you know, multiply by time and just integrate and get the mass loss. So the broadcast/tarp has 63 percent, the broadcast/untarp has 62 percent, the bed/untarp is 61, and the bed/tarp is 68.

PANEL MEMBER GLANTZ: So they're all about the same.

DR. BARRY: Yeah.

PANEL MEMBER BLANC: Interesting.

DR. BARRY: So, anyway, the way -- so this gives you a sense of how the flux affects later your estimates. And the reason that the broadcast/untarp is our driving variable for the short exposures is because of that high peak there. That's a six-hour average. So we're using that number.

And then the 24 hour is an average of four of the highest dots down there in the bed/tarp.

--o0o--

DR. BARRY: Okay. I had said that our air concentrations for screening mode are dependent on the averaging time in the flux. And we only have six-hour estimates. We need a one-hour concentrations for

chloropicrin. So we're going to use what's called a peak-to-mean estimation. And the reason that we can do that is because the mean concentration of any water, or air for that matter, that's measured is a time-weighted average and it's a result of many short-term peak concentrations. And you can calculate a definable relationship between peaks and means. And you can actually do a first principles relationship but it's very complicated.

You can also do empirical relationship. And in 1968, Hino looked at empirical data and found that definable relationship for air concentrations with the sampling time ratios between 10 and 6 hours could be expressed by the ratio of the sampling time raised to the .5 power. So that's what we used in the Department to do our peak-to-mean estimates based on that paper.

--o0o--

DR. BARRY: So here's a peak-to-mean equation. So one-hour concentrations were estimated using this equation. TP is one hour, TM is six hours. There's the minus 1/2, which is the 1/2 power -- negative 1/2 power law in this case. And what means is our six-hour concentrations are multiplied by a factor of 2.24 to get a one-hour concentration.

I think that's the end of me.

--o0o--

DR. BEAUVAIS: Okay. If that's all clear, I'll present now the exposure estimates. And these based on the modeled estimates that Terri provided.

First of all, we have -- these are bystanders to soil fumigation. And I'll talk about the short-term exposures first.

These again are the highest model concentration for each interval. Terri provided me exposure estimates for each of the application methods. And what I'm reporting here is, out of all of those, which were the highest?

And the assumptions again that went into these were 40 acres and the maximum allowed application rate on the current product. So we assumed that concentration is proportional to application rate. So when the -- I did an adjustment for that from the application rate that was used in the studies.

So we have, for one hour the concentration is 110 --

PANEL MEMBER BYUS: I was going to ask you that on the other slide where you did have the one bit of experimental data where it was half the application rate. But it's consistent, or there is direct relationship?

DR. BEAUVAIS: Approximately, yeah.

PANEL MEMBER BYUS: Experimentally is what I'm -- I mean that was the --

DR. BEAUVAIS: I have to turn to the --

PANEL MEMBER BYUS: Experimentally.

DR. BARRY: You mean measured -- you mean like an experiment --

PANEL MEMBER BYUS: -- those curves and a few -- I mean it was consistent. You would have predicted.

DR. BEAUVAIS: Do we have --

DR. BARRY: If they changed -- okay. You're asking the relationship between application rate in flux or between flux and --

DR. BEAUVAIS: Application rate in flux.

PANEL MEMBER BYUS: Well, right. Well, rate over time.

DR. BARRY: Okay. I need --

PANEL MEMBER BYUS: But she just said -- I mean you're trying to get the --

DR. BEAUVAIS: I've adjusted for application rate. And then he's wanting to know if there's data to support that.

DR. BARRY: We haven't done a study on that.

PANEL MEMBER BYUS: You took the 500 appli -- most of the data was at 500, so that's probably what you used to do your modeling.

DR. BARRY: Oh, no, no. The data was at 80 pounds, 171 pounds.

PANEL MEMBER BYUS: Okay.

DR. BARRY: Yes, yes, yes, yes. And we do make the assumption -- well, we know that flux is -- air concentrations are directly proportional to flux. And we do make the assumption that flux is proportional to application rate. And that's the general assumption that's made in these studies. We have not experimentally demonstrated that ourselves.

DR. BEAUVAIS: So I'm reporting concentrations both in micrograms per cubic meter and parts per billion because the concentration measurements were all reported in micrograms per cubic meter. And then when we turn over to the toxicity data, those are all in parts per billion. So just to make that conversion. Once Carolyn gets up here and starts talking, she'll be talking in ppb rather than micrograms per cubic meter.

So the tables in the exposure assessment present both.

So 1 hour is 110,000 micrograms per cubic meter, 8 hours is 44,000, and 24 hours is 7,400. Those are the exposure estimates, the screening estimates for bystanders to soil fumigation.

--o0o--

DR. BEAUVAIS: And then for context I'm also -- remember, I showed you the use -- those figures that showed that, you know, we were roughly at 80th percentile for the 40 acres and above the 99th percentile for the 500 pounds per acre application rate. So this is a 50th percentile exposure, again at the field edge. So that in this case, basically this shows us what happens if we have a smaller application at a lower rate.

And so these -- and there are a series tables back in Appendix 3 in the document that look at variations of this and, you know, different distances and such as well.

And as you can see, if you decrease the application rate and the application size, our concentration estimates go down quite a bit.

--o0o--

DR. BEAUVAIS: And then this is -- assuming these first two tables were looking at the field edge, this is looking half a mile away. So the buffer zones that EPA is proposing range from 25 feet to half a mile. And so if you were to go as far as you could go with the data that we have and assuming these 50th percentile applications, again the concentrations decrease quite a bit.

PANEL MEMBER BLANC: But they're still not trivial.

DR. BEAUVAIS: They're still -- yeah, they're still up there.

PANEL MEMBER GLANTZ: I mean 25 feet just seems sort of silly.

DR. BEAUVAIS: Well, the 25 feet were -- those are based on the size of the application and the amount of chloropicrin used. So those would be like orchard applications where you're using a hand wand into an individual hole. That's where you'd be looking at 25 feet.

PANEL MEMBER HAMMOND: And that could be worker bystander, right?

DR. BEAUVAIS: They could be worker bystander or --

PANEL MEMBER HAMMOND: But that 25 feet makes sense for worker bystander?

DR. BEAUVAIS: Yeah. Well, when EPA is talking about a 25-foot buffer zone requirement, those are very small applications.

PANEL MEMBER HAMMOND: Oh, that is for the community?

DR. BEAUVAIS: Yeah, it is. Basically they're requiring that you be 25 feet away from anyone, dwellings and such as well.

PANEL MEMBER BLANC: No. But I do think that the

salient feature here, for example, is that even at half a mile away and even at the 50th percentile application, you have 1.1 part per million one-hour exposure that you're modeling. So these are substantive exposures even --

CHAIRPERSON FROINES: I'm sorry. Paul, you said 1.1 --

PANEL MEMBER BLANC: -- part per million.

PANEL MEMBER HAMMOND: -- ppm, yeah, part per million.

PANEL MEMBER GLANTZ: If you take 1100 and divide by a thousand.

(Laughter.)

--o0o--

DR. BEAUVAIS: Okay. And, again, just to talk about the uncertainties associated with this, in which are -- then we have the appraisal section at the back of the document where we talk about those and just a few of the key assumptions, that we assume that 40 acres treated per day is a practical maximum. We do note that if more than one rig is used, you could treat more acres. And we don't have a sense of how often that happens. And as I showed you in that figure, the PUR data suggests that 40 acres per day is about 80 to 85th percentile of all application. But that's also recognizing that some of those applications probably span multiple days.

And also, adjustments for application rate assume that flux in concentrations are proportional to application rate. And I also -- just sort of a caveat here, that all of our adjusted concentrations are outside the measured range. So, anyhow, anytime you're doing that, that adds some uncertainty as well.

--o0o--

DR. BEAUVAIS: Okay. And that was the short-term exposure estimates. And now I'm going to talk about the seasonal, annual, and lifetime exposures.

And those monitoring in several of these studies span as long as two weeks. And that allowed us -- so we had a two-week data set to work with. And what Terri did there was she averaged a 24-hour flux calculated over that. So it was a moving 24-hour average ore that two-week period. And because wind direction is not constant over these longer intervals, which is what you were talking about just a little bit ago here as part of the discussion here, concentrations were adjusted sort of in the opposite direction, if you will, but using a time scaling factor that's based on that peak-to-mean theory. So whereas we we're going from six hours to one hour, we increase the concentration; when we're stretching the longer intervals, we decrease the concentration using a factor like that.

And when we're talking about these longer Appli -- or these longer intervals concentrations, exposures are not adjusted for maximum application rate. So we're not assuming that somebody's consistently next to 500 pounds AI per acre, which again fits with what we see in the pesticide use report data.

PANEL MEMBER BYUS: Say that one more time.

DR. BEAUVAIS: Okay. For the short-term exposures we --

PANEL MEMBER BYUS: Just the last part. I mean the -- obviously the people in the apartment were near the --

PANEL MEMBER HAMMOND: But these are the seasonal, annual, and lifetime. I think that's the --

PANEL MEMBER BYUS: Okay.

DR. BEAUVAIS: Yeah. And so what I'm saying is that unlike the short-term exposures, these -- we're not adjusting these upward, we're not assuming that somebody's consistently against a high-end application. They could be against --

PANEL MEMBER BYUS: Theoretically someone could be in that apartment building for two weeks. But then you're looking at -- Okay. But you're using the two-week data to go seasonally.

DR. BEAUVAIS: Exactly, exactly.

PANEL MEMBER BYUS: I'm sorry.

DR. BEAUVAIS: Yeah, the two --

PANEL MEMBER BYUS: Right. Very good, very good. I didn't listen carefully enough.

DR. BEAUVAIS: Sorry.

Okay. And then the length of the season is approximated using PUR data from the top four counties. And I'll show you that now.

--o0o--

DR. BEAUVAIS: These are the top four counties where chloropicrin is used. These are Monterey, Ventura, Santa Barbara, and Santa Cruz counties. And the idea behind this is that you could have people that move up and down, worker bystanders, for example, strawberry grower -- I'm sorry -- strawberry pickers or people harvesting strawberries that may move from Ventura on up the coast and following the strawberries, and that your applications may follow that. Now, we don't have a sense of, you know, whether the -- how close they are actually to these applications. And, you know, so we have some uncertainty that we introduce in using the Pesticide Use Report data, because, you know, whether somebody is actually where the applications are happening all the time is another question entirely. But --

PANEL MEMBER GLANTZ: Do you just -- in a field

would you only apply this once, or do they do repeated applications?

DR. BEAUVAIS: There are some cases where they would do twice. But in most cases it's once.

PANEL MEMBER GLANTZ: So it's once per season?

DR. BEAUVAIS: Yeah. And with strawberries it's once -- yeah, once per crop. And then they fumigate between crops, yeah.

PANEL MEMBER GLANTZ: How many crops are there per season?

DR. BEAUVAIS: Most cases one. And you can have two.

PANEL MEMBER BLANC: You should point out that this is a modification --

DR. BEAUVAIS: Yes.

PANEL MEMBER BLANC: -- from the previous draft document.

DR. BEAUVAIS: Yeah.

PANEL MEMBER BLANC: Which had the season being --

DR. BEAUVAIS: -- based on Monterey County only.

PANEL MEMBER BLANC: -- three months, is that right?

DR. BEAUVAIS: Four months, yeah.

PANEL MEMBER BLANC: It was four months. So

it's --

DR. BEAUVAIS: So basically what happens when you add -- yeah, when you -- I'm sorry. Yes. When you add in these additional counties, it stretches out the season a little bit. So we go from four months to five. Basically what happens is Ventura, down when you get a little further south, applications are happening earlier. And the season's happening earlier basically. So that caused June and July to go up and November to go down when we averaged across all four counties.

But the idea behind this is what -- I need to describe the graph briefly here too. This is -- across the bottom here are the months of the year. And these are five-year averages of use reported in these counties for these months. And then the Y axis is percent of annual use based on pounds applied. And so we're making the assumption here that exposure's most likely when use is happening or less likely to happen when there's not as much use.

So that's -- and I'm setting a cutoff of 5 percent of the annual use. And so when I do that, I have five months. And so that's the seasons that I'm using for the bystanders here.

--o0o--

DR. BEAUVAIS: And then so bystanders to soil

fumigation. The seasonal exposure includes one week to a year. And then annual and lifetime are explanatory.

So our assumptions again are 40 acres treated, and then that applications occur roughly every two weeks over five months during that year.

And then the annual concentration is calculated by taking that seasonal and then multiplying it by 5 over 12.

So I also changed the assumed application rates. And I went -- rather than assuming 500 pounds AI per acre for the seasonal and annual, I went with 350 pounds AI per acre. This is what EPA assumed it's based on the amount that's supported by registrants. And you're still well above the 50th percentile here, but it's not quite 500.

And then we go to lifetime. I did use the actual 50th percentile application rate for that. But all of this is assuming 40 acres.

So the concentrations that we get were: For seasonal 490 micrograms per cubic meter, annual was 200, and lifetime was 88 micrograms per cubic meter for soil fumigation bystanders.

--o0o--

DR. BEAUVAIS: So with the exception of the application rate, the assumptions that we used were the same for these longer term as for the short-term

estimates. They were not adjusted for the maximum application rate.

And also, as I mentioned, that you could have multiple applications in some areas. And looking at the Pesticide Use Report data, we do see some sections, some of these one-square-mile sections where you can have frequent applications as much as 38 days over a five-month interval. How close they are to each other and how close bystanders are to any of these, I don't know. But, again, the PUR data only allow me to go to one -- a resolution of one square mile.

--o0o--

DR. BEAUVAIS: So that was it for soil fumigation.

If there aren't any more questions, I'll proceed to structural fumigation bystanders.

PANEL MEMBER BLANC: Yeah, you have about ten minute more, you think, for presentation?

DR. BEAUVAIS: There are about 11 more slides -- I'm sorry -- 10 more slides, yeah.

PANEL MEMBER BLANC: And then we should take a break after that for our transcriptionist. Are you okay?

CHAIRPERSON FROINES: That's what I was about to ask.

PANEL MEMBER BYUS: Maybe we could start a

bonfire in here, warm it up a little bit.

The temperature is -- it's cold in here. The temperature is cold.

Are we all cold or a little chilly?

MR. MATHEWS: There's no budget.

PANEL MEMBER GLANTZ: I'm comfortable because I have a protective layer of fat.

(Laughter.)

DR. BEAUVAIS: Okay. So in addition to the soil fumigation, as I mentioned before chloropicrin is also used as a warning agent in structural fumigations. And we do have studies in which off-site concentrations were measured during structure fumigation. And so we have three studies conducted by ARB and one study conducted by registrants. And as it turns out again, the highest concentrations for chloropicrin occurred in that registrant study. So I'm going to be focusing on that one as I describe this to you. All the studies are described in the document.

But the --

PANEL MEMBER HAMMOND: That study's new from the --

DR. BEAUVAIS: Yes, you're right, that is the new study.

PANEL MEMBER HAMMOND: That's the new study,

right?

DR. BEAUVAIS: Yes. But we received that study within the last year or roughly about a year ago.

So, I just want to point out that the amount of chloropicrin used is much lower for structure fumigations than soil fumigations, and that it's only used as a warning agent. So we're talking about smaller amounts of chloropicrin and smaller areas being treated. And you're not taking acres here. You're talking individual structures.

--o0o--

DR. BEAUVAIS: So this is a description of the study. Basically they monitored eight fumigations. They had four houses. And in each house, they tarped it, fumigated it, aerated it, took the tarps down, and then repeated that process. So that each house was fumigated twice and back to back like, one after the other.

And then they had a total -- around each house a total of 32 samplers. All were set around on the outsides. And they -- they reported concentrations during the fumigation and then during the aeration,

And then once the aeration was completed, they switched over to indoor samplers. And I'll talk about those when I'm talking about the indoor concentrations.

But right now focusing on the outdoor samplers,

they were set up around the house -- sides and corners of the house, so you had two to six samplers on each side. And I'll show you here.

--o0o--

DR. BEAUVAIS: So this is one of the houses here. And each of these letter-number combinations corresponds to a sampler. So here you have the 2 and 4, and then here we go 1 out through 8. And so in these samplers the 1 and 2 numbers are five feet away from the edge of the house, and the 3 and 4 are ten feet away. Number 5's are 25 feet away, 6 is 50 feet, and on up to 8's, which are 100 feet away from the house. So on four sides here we had a hundred feet away.

And so this is -- the house that I'm showing you here is the Replicate 2, which is the second fumigation of the first house that they did. And this is where the highest outdoor concentration came from. And so the samplers were collected during the 24-hour fumigation and the 12-hour aeration that followed that.

The highest outdoor chloropicrin concentrations were measured following the second fumigation of the first house. This is roughly a 32,000 foot cubic -- 32,000 cubic foot house, and it occurred at the sampler five feet west of the house here.

--o0o--

PANEL MEMBER GLANTZ: Was the wind blowing?

DR. BEAUVAIS: A little bit. What I have are averages for these sample intervals. That's what was reported in there. Well, they actually did give me five-minute averages as well. But they averaged over time. And so I have -- in there I've reported I think that information.

So based on this, results were adjusted for field spike recoveries. Now, what they did was these were fumigated with sulfuryl fluoride. And then chloropicrin was used at the rate that the labels tell you to use this. So I didn't adjust for that. So it was adjusted for field spike recoveries.

And in terms of structure fumigation, you tend to fumigate a house pretty rarely. And you don't run around and fumigate one after another in a neighborhood. So we're not dealing with seasonal, annual, or lifetime exposures here. So these are only short-term exposures.

And so one hour is 244 micrograms per cubic meter, on down to the 24 hour which is 49.7 micrograms per cubic meter.

--o0o--

DR. BEAUVAIS: In addition to the structure -- so that's it structure fumigation. And in addition to that, we also have a space fumigation. There is a single

product label that's got bystander -- or that has directions for fumigating in closed spaces. And it's for empty potato storages and grain bins. So potato warehouses and grain bins. And EPA has received a request from the registrant to cancel the registration. However, that label's still active, so it's considered an exposure assessment.

The maximum application rate is .7 pounds chloropicrin per a thousand cubic feet. And I'm assuming a use of twice per year; that you fumigate between crops and that you have two crops per year.

And so I have a 24 -- the annual then is the 24-hour concentration times two days divided by 365.

--o0o--

DR. BEAUVAIS: So what I did was I used the structural fumigation data and expanded toward a larger size so more chloropicrin being used, larger application rate and larger size.

But I don't have seasonal exposures because I don't have any duration anticipated between a week and a year. So the one-hour adjacent to one of these is estimated at 160,000 micrograms per cubic meter; and eight hours is 46,000; and 24, 34; and then on down to annual and lifetime, which are both 190.

--o0o--

PANEL MEMBER BYUS: You said this is just the internal space that's being fumigated.

DR. BEAUVAIS: Yeah.

PANEL MEMBER BYUS: Like this is no bystander, this is just the --

DR. BEAUVAIS: No, these are bystanders. These are adjacent.

PANEL MEMBER BYUS: These are bystanders?

DR. BEAUVAIS: Yes.

PANEL MEMBER BYUS: So this is not the internal concentration --

DR. BEAUVAIS: No, these are adjacent --

CHAIRPERSON FROINES: No, it's bystanders.

DR. BEAUVAIS: So it's scaling up from that structural fumigation data.

PANEL MEMBER GLANTZ: But is it still -- I mean when you talk about an annual exposure, I mean is it still emitting over a year? So you're taking --

DR. BEAUVAIS: I'd say over a year you're getting these pulsed exposures.

PANEL MEMBER HAMMOND: They may refumigate the deep potato bin.

DR. BEAUVAIS: Yeah.

PANEL MEMBER HAMMOND: Where they fill it up with potatoes and they empty it and they refumigate it?

DR. BEAUVAIS: Yeah.

PANEL MEMBER BYUS: I mean I -- so the actual concentration in the bin, out of curiosity, I mean what does it take to kill off the fungus or whatever you're killing in there?

(Laughter.)

DR. BEAUVAIS: I've got a --

PANEL MEMBER BYUS: Compared to what -- it's interesting. I mean I --

PANEL MEMBER HAMMOND: Well, maybe it was .7 pounds per --

DR. BEAUVAIS: Yeah, it's -- that's the application rate, so I can -- yeah, I actually have a spreadsheet where I've put that into parts per billion. But I haven't put it in the document and I don't the number off -- it's hundreds of thousands, but -- it's substantial, the internal concentration is --

PANEL MEMBER BLANC: Can I ask on the previous -- now let's leave the storage bin aside for a second and talk about the structural. The data that you had from the one home that's presented earlier on in the document, where at two weeks it was two parts per billion and then at 12 weeks it was still two parts per billion. Do you know what I'm referring to? Was that --

DR. BEAUVAIS: Structural?

PANEL MEMBER BLANC: It was a structural application somebody may -- I think you cited apropos.

Now, wait. Maybe it's the other -- oh, no, it's actually in the health assessment. It's about a family that had symptoms of the Teslaa article.

DR. BEAUVAIS: Okay.

PANEL MEMBER BLANC: And chloropicrin residues measured at 6, 18, and 38 weeks after application were 30, 2, and 2 parts per billion.

Does that at all affect the calculations that you would make for what the outside bystander exposure might be from a household application? In other words, if these data suggest that inside there's still detectable chloropicrin a month and a half after, so there would be some flux outside. I think that your --

DR. BEAUVAIS: Oh, I see what you're saying. So in other words the fact that I'm saying that there's no --

PANEL MEMBER BLANC: Yeah, 24 -- there's no seasonal, for example. Is that, strictly speaking, true based on those data?

DR. BEAUVAIS: Yeah, it's a -- it's a good question.

PANEL MEMBER BLANC: You might want to just pull that article and look at it, because I guess it's partly because it was dealt with in the health section that you

didn't hone in on it.

DR. BEAUVAIS: Yeah.

PANEL MEMBER BLANC: Maybe there was something peculiar about the --

DR. BEAUVAIS: Well, I'm trying to remember it and trying to remember if we haven't -- if there's a chance that that was not a legal application. And perhaps that was an over application, but I don't know. But, yes, I'll look at that.

PANEL MEMBER BLANC: Okay.

DR. BEAUVAIS: Moving forward again.

Okay. So that's what I was just showing you, a space fumigation.

--o0o--

DR. BEAUVAIS: And then to talk about the uncertainties associated with structural and space fumigation, that in this case we base concentrations on measured off-site data, not modeling. In this case, they probably expected to be health protectives because the samplers were -- unlike the situation with the field applications, these studies were monitoring actual applications where the samplers were roughly as close as the bystanders are expected to be. And they were going at maximum application rates.

And then I corrected for field spike recoveries.

--o0o--

DR. BEAUVAIS: And then, finally, the last thing to talk about is indoor air concentrations, which is something that the toxic air contaminant regulations specify that we do need to address. And in the case of chloropicrin indoor air concentrations, not -- all bystanders we don't distinguish between outdoor and indoor. I'm not making any assumption that if the house is adjacent to a field, that the concentrations have decreased somehow within the house. And we're not making any assumptions about that. So we're sort of factoring that in and implying it, you know, in an unspoken way in the document with all the bystander estimates.

But for indoor concentrations people can enter a structure that has been fumigated and we have data to suggest that there could still be chloropicrin concentrations that they could be exposed to after that. And so what we're looking at here is in this study's -- in the registrant study they had indoor air concentrations post-aeration. So this was after the houses were cleared. And when they clear them they look at the fumigant. They don't look at the chloropicrin concentrations. They go in and they measure the fumigant and say in this case sulfuryl fluoride concentrations are below the prescribed amount to allow people back in. And that's the point at

which it's considered cleared.

And so this is the point at which they began measuring. And so these are representing people entering a treated structure.

And in this study they had four samplers in each house. And this is the house that had the highest indoor air concentrations. And in this case they had samplers in a bedroom, a utility area, a crawl space, and in an attic. In some of the houses they also had a living room and a bedroom, for example.

--o0o--

DR. BEAUVAIS: And so the highest indoor concentrations were in Replicate 4, which was the second fumigation of the second house, and that for the 1 hour. And then Replicate 5, which would be the first fumigation of the third house, 8-hour and 24-hour concentrations. And in this case, again results were adjusted for field spike recoveries.

And the 1-hour concentration is 3,060 micrograms per cubic meter, on down to the 24-hour, which is 1,160. In this case they did have -- and the ARB studies didn't show substantial concentrations after aeration. But in this -- we did have in this study some fairly high concentrations.

PANEL MEMBER BLANC: And they only went out to 24

hours is what you're saying?

DR. BEAUVAIS: Yes.

PANEL MEMBER BLANC: But you could calculate a half-life based on going from 180 to 170 over the next 16 hours, the way it did, right? I mean the half-life must be something like six days or seven days or something, or more.

DR. BEAUVAIS: Um-hmm.

PANEL MEMBER BLANC: So that would probably let you come up with a more than 24-hour exposure calculation for the indoor, right?

DR. BEAUVAIS: Okay.

PANEL MEMBER BLANC: I mean the area under the curve must be considerable.

CHAIRPERSON FROINES: Yeah.

PANEL MEMBER BLANC: So in fact there probably is something that's like a seasonal value that's going to be not trivial.

DR. BEAUVAIS: Okay.

CHAIRPERSON FROINES: I don't want to take questions right now. I'd rather we take a break, because it's 11:35. So we've been going for at least two hours.

So let's take a break, Joe, and then we can start asking questions.

So let's take a ten-minute break.

(Thereupon a recess was taken.)

CHAIRPERSON FROINES: Folks, are you -- but you're not ready.

DR. BEAUVAIS: I'll stop chewing.

PANEL MEMBER BLANC: Now, here's what I'd recommend. I know that you had some questions. But what I think we should do is just hear the health presentation and then sort of integrate our questions at that point.

CHAIRPERSON FROINES: But it may be -- now, you realize it may be that the questions -- with your 2 o'clock timeline, and it's 12 o'clock, will we have -- what I'm worried about is having to wait to another session before we get to questions asked.

PANEL MEMBER BLANC: Well, let's just -- John, I don't know how many questions you have.

PANEL MEMBER LANDOLPH: I can certainly wait. Because we're going to do another one, right, before we finish here?

CHAIRPERSON FROINES: Yeah, but I don't want you to forget. I mean I --

PANEL MEMBER GLANTZ: Why don't you let him ask his questions.

PANEL MEMBER LANDOLPH: I have a memory like an ox.

CHAIRPERSON FROINES: Why don't we just go around

with questions. And if it starts to look -- if we run more than a half hour, we'll stop and go with Paul's suggestion.

Let's just see who has questions.

So, Joe, start out.

PANEL MEMBER LANDOLPH: Yeah, thank you for your presentations. They were very thorough. I had a couple quick questions.

One is, are there not alternatives to chloropicrin as a marker? I guess it's used because it's very accurate at low concentrations. Aren't there more benign substances, thiols or something, that could replace it? - is one.

DR. BEAUVAIS: To answer that question, that hypothetical, there certainly ought to be. And I don't -- we don't have any that I'm aware of right now. I mean it's difficult to have something that has a sharp response rapidly. And chloropicrin does that. But that is -- yeah, that certainly is some technology that would be nice to have, is a change in chemicals, yes, for --

PANEL MEMBER LANDOLPH: Okay. And then another one is, I looked over the manufacturers', scientists', you know, comments and your questions, and I read that very carefully. And certainly there is data for mutagenicity in bacteria and --

DR. BEAUVAIS: Okay. That's different --

PANEL MEMBER BLANC: Joe, can I interrupt you. I think that's going to be appropriate to the health effects part that we're about to hear.

PANEL MEMBER LANDOLPH: Okay. Well, that's all the questions I've got on that section. So go ahead.

DR. BEAUVAIS: Okay.

CHAIRPERSON FROINES: Craig.

PANEL MEMBER BYUS: I asked most of my questions. But just echoing him, I'm a nongenotoxic marker would be what I would go try and find, something that was not genotoxic, if at all possible.

CHAIRPERSON FROINES: Can I make a comment from -- is Marylou in the room?

DPR ASSISTANT DIRECTOR VERDER-CARLOS: Yes.

CHAIRPERSON FROINES: Marylou, at some point I think it would be great -- it would be very advantageous if we had a session that was a sort of thinking session, because I think the subject of fumigants deserves a lot of discussion. And it would be nice to have just an open-ended session where we all sort of exchanged ideas about these kinds of things that come up. And nobody needs to worry, because it would be just ideas being discussed.

DPR ASSISTANT DIRECTOR VERDER-CARLOS: I agree

with you. So I'll keep -- actually internally we were planning on doing that for all fumigants already, but --

MR. MATHEWS: It's on the record. She has to be on the mike so we can get it on the record.

CHAIRPERSON FROINES: I don't want to take -- so we can let it go if you want.

DPR ASSISTANT DIRECTOR VERDER-CARLOS: Oh.

CHAIRPERSON FROINES: We can let it go if --

DPR ASSISTANT DIRECTOR VERDER-CARLOS: We'll just --

CHAIRPERSON FROINES: Go over and say yes.

DPR ASSISTANT DIRECTOR VERDER-CARLOS: Yes, I agree with you, Dr. Froines.

CHAIRPERSON FROINES: I still lecture in my classes at UCLA on DBCP and, you know, it's been a long time since -- so the issue is really still with us in a big way.

So in a kind of semi-formal, informal meeting it would be interesting to talk about these kinds of issues. And it might even be interesting to have some people who know something also outside --

PANEL MEMBER GLANTZ: We should talk about this after Paul leaves.

CHAIRPERSON FROINES: Yeah, that's what I'm trying to -- I'm trying to stop. I'll stop. I made my

point.

Paul.

PANEL MEMBER BLANC: I asked the questions I had during the session.

CHAIRPERSON FROINES: Kathy.

PANEL MEMBER HAMMOND: Likewise.

PANEL MEMBER GLANTZ: I already asked my questions.

PANEL MEMBER FRIEDMAN: I have no other questions.

PANEL MEMBER BYUS: I might also just compliment you and say what a nice job you did presenting this data.

DR. BEAUVAIS: Thank you.

PANEL MEMBER BYUS: Thorough, it was. The nice data sets to back up the modeling. It was very nice to see.

DR. BEAUVAIS: Thank you.

DR. BARRY: Thank you.

DR. BEAUVAIS: We appreciate the help that the leads have given us on this too. Thank you.

PANEL MEMBER HAMMOND: Yeah, I agree though with Craig. It was a wonderful presentation, clear for complicated material.

DR. BEAUVAIS: Thank you.

CHAIRPERSON FROINES: We've already talked. But

it shows you the benefit of good leads working with the agency.

PANEL MEMBER HAMMOND: No, the agency gets the credit.

PANEL MEMBER GLANTZ: Let's move on. Let's move on before Paul Blanc strangles someone.

DPR ASSOCIATE TOXICOLOGIST LEWIS: With that, I will move on.

(Thereupon an overhead presentation was Presented as follows.)

DPR ASSOCIATE TOXICOLOGIST LEWIS: As many of you know, chloropicrin was used as a warfare agent in World War I primarily due to its strong ocular and respiratory irritant properties. It was first used as a fumigant in 1926 in flour mills.

NIOSH established the immediately dangerous to life and health level at 2 ppm based on reports that soldiers were incapacitated or unable to fight at these concentrations.

The threshold limit value was set at .1 ppm based on reports of tearing at .3 ppm. DPR placed chloropicrin --

CHAIRPERSON FROINES: Question.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yes.

CHAIRPERSON FROINES: California updates their

TLVs annually. So is the ACGIH TLV and the California value the same?

DPR ASSOCIATE TOXICOLOGIST LEWIS: No. There's the RELs, if you're referring to OEHHA's RELs, or --

PANEL MEMBER HAMMOND: Cal/OSHA.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Cal/OSHA. Yeah, I'm not -- actually, to be honest, I'm not aware of what Cal/OSHA's TLV is for chloropicrin. But I can certainly --

CHAIRPERSON FROINES: It's not a big deal. It's just --

PANEL MEMBER FRIEDMAN: Could you just tell us what TWA and TLV stands for?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Time weighted average, threshold limit value.

PANEL MEMBER FRIEDMAN: And limits for health or what?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Well, it's usually an occupational exposure limit that --

PANEL MEMBER HAMMOND: And, yes, it's a health based. It's the -- this is where the OSHA regulations came from originally. These are the industrial hygiene organizations' recommended values before there was an OSHA.

CHAIRPERSON FROINES: It's a maximum value for --

PANEL MEMBER HAMMOND: And it's supposed to be the level at which workers have been exposed for 40 hours a week without adverse health effects.

PANEL MEMBER FRIEDMAN: Oh, okay.

CHAIRPERSON FROINES: But it's an 8 hour --

PANEL MEMBER HAMMOND: Yeah.

CHAIRPERSON FROINES: Onward.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. Moving on.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. Chloropicrin was placed in reevaluation based on air monitoring data that showed that the air concentrations exceeded the TLV at some distances from greenhouses that were fumigated with chloropicrin.

The primary effects seen in animals and humans with exposure to chloropicrin are sensory irritation and respiratory toxicity. And one of the proposed mechanisms for this toxicity is its reaction with various biological files. And this diagram shows the reaction of chloropicrin on the left there, with glutathione above and with hemoglobin down below. This results in the formation of disulfide bridges and the formation of dichloronitromethane.

Yes.

CHAIRPERSON FROINES: Go ahead.

PANEL MEMBER LANDOLPH: Okay. Real quick.

Is that driven by glutathione tranferase or is that just a spontaneous reaction?

DPR ASSOCIATE TOXICOLOGIST LEWIS: I think it's a spontaneous reaction.

PANEL MEMBER LANDOLPH: Because I didn't see any mention of glutathione transferase that would --

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah, I was not aware. There are very few studies on the metabolism or toxicity mechanisms for chloropicrin. And --

CHAIRPERSON FROINES: Can I comment on this?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Uh-huh.

CHAIRPERSON FROINES: This is a very nice picture that Susan Sparks at UC Berkeley did in 1997, I think, and in 2000. And what's not -- why she's not quite correct in what she's doing -- it's a nice piece of work. But the chlorines on the compound are electron withdrawing. So's the nitro group. And so what you've got is a very strong partial positive charge on the carbon. And there is -- there is literature showing, for example, that methanol that's been treated with sodium and forms an anion will react also with chloropicrin. In other words, chloropicrin is a strong -- is a strong electrophile that produces irreversible covalent bonds, and that

this -- this is just showing its electrophilicity. This is not a mechanism for toxicity. This is -- this shows that carbon has got a partial positive charge and will react with thiols and will react with a whole bunch of other things that are nucleo-thiols.

And so it's -- if you understand the chemistry, we need -- this comes up because of the genotoxicity and carcinogenicity. If you add a third feature, which is the electrophilicity of the compound, that adds to the notion of electrophilicity. And I saw your -- I saw that paper -- those two papers that you quoted, and I thought that was very good. But I think that carbon is very reactive.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. Some of the other proposed target proteins are succinate and pyruvate dehydrogenase, which have thiol groups in their active site. Inhibition of these enzymes is supposed to be -- or is suspected to be the cause of the lacrimatoried effects of chloropicrin. Also, inhibition of these enzymes correlates with the lethality of other halonitromethanes, quinones, fungicides, and other thiol-reactive chemicals.

Did you want to go back?

PANEL MEMBER BLANC: No, just to sort of translate John's comment into a practical editorial

modification of the section -- this section on pathways of reaction. I think to just -- the problem could be addressed by simply a sentence at the end of that section just before the beginning of the acute toxicity, you know, that would say, "In summary, this compound is" -- "this electrophilic compound is capable of multiple reactions, of which these are examples but are not meant to be the sole substrates with which chloropicrin can react."

CHAIRPERSON FROINES: Doesn't have to just react with proteins. It can react with nucleophiles that contain nitrogen as well as sulfur.

And just --

PANEL MEMBER BLANC: No, I think, John, if you have -- I don't think that that sentence or two sentences needs necessarily to have a reference. But if you had one, you want to pass on to the --

CHAIRPERSON FROINES: Well, I'll give you the reference from the 1966 paper that shows the reactivity -- its reactivity.

PANEL MEMBER BLANC: So I don't think you in any way need to rewrite the section. I Just think you need to say something pithy at the end of that section, say "These are examples. This isn't meant to be," you know --

DPR ASSOCIATE TOXICOLOGIST LEWIS: -- limited to that.

PANEL MEMBER BLANC: Right.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah. Okay.

CHAIRPERSON FROINES: It sure reacts with thiol groups though.

DPR ASSOCIATE TOXICOLOGIST LEWIS: I'd just like to interject before I go on to this slide.

Dr. Blanc had mentioned earlier -- wondered if I had some comments to make about the Maine manufacturing incident. I was not aware of that study until recently. So it isn't in the current draft of the document. I'll look at it to see if there's some illness reports in it that would be useful.

PANEL MEMBER BLANC: Main manufacturing, I'm sorry, you lost -- oh, the Maine, Maine, the State of Maine.

DPR ASSOCIATE TOXICOLOGIST LEWIS: The State of Maine, yeah, not --

PANEL MEMBER BLANC: Right, right.

(Laughter.)

PANEL MEMBER BLANC: Although it is described in the health section elsewhere -- no, it's not actually.

DPR ASSOCIATE TOXICOLOGIST LEWIS: I don't think so. No, I didn't --

PANEL MEMBER HAMMOND: I think the environmental --

DPR ASSOCIATE TOXICOLOGIST LEWIS: It's in her document and not in mine.

PANEL MEMBER BLANC: All right. Good. Thank you.

CHAIRPERSON FROINES: One thing I wanted to comment on was, there's a paper this year, 2007, 2006, 2008, that looks at the issue of academic research and the quality of academic research versus good laboratory practices. And it's a devastating paper. And I'll send it to you --

PANEL MEMBER GLANTZ: Who's stating to which side?

CHAIRPERSON FROINES: Good laboratory practices are -- is the equivalent to prehistoric animals.

(Laughter.)

PANEL MEMBER HAMMOND: It's good for dinosaurs?

CHAIRPERSON FROINES: It's good for dinosaurs.

PANEL MEMBER BLANC: Okay. We should move on now. Okay?

CHAIRPERSON FROINES: No., but it's an important issue for her to -- I don't think she's seen that paper. And so she --

DPR ASSOCIATE TOXICOLOGIST LEWIS: I might not have.

CHAIRPERSON FROINES: It will be useful just to

make sure -- to understand that --

PANEL MEMBER BLANC: Okay.

DPR ASSOCIATE TOXICOLOGIST LEWIS: So, a human sensory irritation study was conducted for chloropicrin. And this study was used to estimate a one-hour NOEL. I'm going to discuss it in some details because of the relevance of the species, also because of its unique design. And benchmark dose analysis needed to be done to come up with a one-hour NOEL.

There were three phases in this study:

The first phase consisted of brief exposures to establish thresholds for odor, eye, nose, and throat irritation.

The second phase involved longer exposures of 20 minute and a chamber at lower concentrations to estimate the ability of subjects to detect the presence of chloropicrin by eye, knows, and threat irritation.

And then the last phase consisted of one-hour exposures over four consecutive days, and which not only the eye, nose, and threat irritation were evaluated, but various respiratory variables and pulmonary function were evaluated.

DPR found this study acceptable because it was conducted according to good laboratory practice regulations and the protocol was approved by the internal

review board at UC San Diego. The protocol was also reviewed by a biostatistician to ensure there was sufficient statistical power. And it was also reviewed by U.S. EPA's Human Studies Review Board and found to be conducted ethically and scientifically valid.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: So the third phase of this study was used to estimate a one-hour NOEL. This study used 32 young adult subjects, 15 of which were male and 17 were female. The subjects were exposed at 0, 100, or 150 ppb for one hour on four consecutive days.

During their exposure, they were asked to rate their eye, nose, and threat irritation on a scale of 0 to 3 every minute during the one-hour exposure.

And at no time was any nose or throat irritation reported. However, eye irritation was reported at both 100 and 150 ppb.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Now, this graph shows the eye -- average eye irritation, broken down by day of exposure. And the top line with the open squares represents 150 ppb level, the black circles represent the 100 ppb group, and the open circles represent the blank air. As you can see, there is no carry-over in the eye irritation from one day to the next

at these concentrations.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: So the eye irritation scores for the four days were average together. And then in this graph, they broke it down by time during exposure. And in this graph, the solid circles are the 150 ppb group and the gray circles are the 100 ppb and the open circles are the blank air.

And you can see after 20 to 30 minutes, the eye irritation scores -- or irritation start to plateau out. The maximum eye irritation scores are reached earlier at the higher concentration, at 100 ppb. They take almost 30 minutes before they reach the maximum.

Also interestingly it at least appears with this data that there's a decrease in the eye irritation during the last five minutes of exposure.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Other respiratory variables were evaluated in phase 3. None of the lower respiratory variables were affected. And this included -- nitric oxide concentration expired pulmonary air. And the nitric oxide is an indication of respiratory inflammation.

There was also no effect on pulmonary function based on the forced vital capacity and the forced

elimination volume in one minute.

However, a couple of the upper respiratory variables were affected. This included a reduction in nasal air flow at 150 ppb and an increase in nitric oxide concentration in expired nasal air at 100 and 150 ppb

CHAIRPERSON FROINES: Just a question.

Paul?

PANEL MEMBER BLANC: Yeah.

CHAIRPERSON FROINES: Would you -- go back to that slide.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Oh, go back one slide?

CHAIRPERSON FROINES: Would you expect -- with this compound, would you expect to see changes in lung function? I wouldn't think it would be sensitive enough.

PANEL MEMBER BLANC: Well, I mean that's a complicated question because it's going to be dose related. So all I would say is that, you know, measuring flow at relatively high lung volumes, they didn't see an effect. There are other more subtle things one can measure, such as changes in nonspecific airway hyperactivity. So all you can say is that these lung function measures didn't show a change. And, again, you're looking at persons who are otherwise healthy. So you can't really comment from these data on whether or not

sensitive -- or susceptible subpopulations would respond differently.

DPR ASSOCIATE TOXICOLOGIST LEWIS: They did purposely exclude people who had allergies or asthma.

PANEL MEMBER HAMMOND: Include?

PANEL MEMBER BLANC: Exclude.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Excluded. I'm sorry. Yeah.

CHAIRPERSON FROINES: I wouldn't be surprised at the NO concentration expiration. There's a pulmonary function I would be more -- well, never mind. Let it go.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. So Table 2 in the document is a summary of the ocular and nasal irritation seen in phase 3 of this study.

The first row shows the average eye irritation score during the entire one-hour exposure period.

And then the second row shows the scores for just the plateau period, which it's defined as minute 30, to minute 55 of exposure.

And the last line shows the average increase in four days for the nitric oxide in nasal air at the different treatment levels.

And because there were effects at the lowest dose level, a benchmark dose analysis was performed to estimate

a NOEL for both of these effects. For the eye irritation, the average score from the plateau period was used to estimate the benchmark doses. The differences were more marked with just limiting it to that period.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: So one of the challenges in doing a benchmark dose analysis with continuous data such as this is selecting the threshold to identify subjects as either responders or nonresponders. We selected a hybrid approach because it was more objective. It uses standard deviation in the control group to establish the threshold.

A benchmark concentration at the 10 percent response level was used for the eye irritation rather than the default of 5 percent because this affect was considered mild and reversible.

However, based on Dr. Blanc's suggestion, we used the 5 percent response level for the increased nitric oxide because of greater concern about this effect.

So the benchmark -- the BMCL at 10 percent for eye irritation came out to 26 ppb by our analysis. And the $BMCL_{05}$ for the increased nitric oxide was 44 ppb.

I would like to point out, in OEHHA's finding, they noted that the reference concentration would actually -- for the increase nitric oxide would actually

be lower than the eye irritation reference concentration, because a smaller uncertainty factor was used for eye irritation since no toxicokinetic variation was anticipated due to a direct acting mechanism of toxicity.

So it may be more health protective to use the increase in nitric oxide concentration for evaluating the one-hour exposures.

However, in the document currently, the one-hour MOEs are calculated using the BMCL for eye irritation.

PANEL MEMBER BLANC: So in other words, if we wanted to compare what would happen with using that more conservative approach with NO, you would essentially divide that by a third?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah, well, have -- the reference concentration for the eye irritation comes out to 8.7. For the increased nitric oxide it would come out 4.4. So it would reduce the MOEs by half.

PANEL MEMBER BLANC: And can you just for our edification clarify -- I'm assuming that there aren't non-parametric alternative benchmark approaches that one can use if it's a non-parametric kind of problem. That's just an assumption I -- I don't think that there is something like that, but I'm just curious. The reason I ask is because certainly for the symptom irritation it's not -- it doesn't -- based on their data, it doesn't

appear to be a normally distributed endpoint. That's why the standard deviations would take you below zero. I mean it's got a long tail.

DPR ASSOCIATE TOXICOLOGIST LEWIS: I'm not aware of any runs for -- that are non-parametric. This was a discussion we had with U.S. EPA. They accepted the chloropicrin task force benchmark dose analysis, which set the threshold at an average eye irritation score of 1.5 as defining a responder or nonresponder. And with that came the assumption that a certain mild eye irritation was acceptable because of its use as a warning agent. We didn't make that assumption.

PANEL MEMBER BLANC: Right.

DPR ASSOCIATE TOXICOLOGIST LEWIS: So --

PANEL MEMBER BLANC: And they didn't use the nitric --

DPR ASSOCIATE TOXICOLOGIST LEWIS: No.

PANEL MEMBER BLANC: -- the nasal nitric oxide. But the fact that they accepted a benchmark approach of any kind means that they weren't dismayed by the -- they didn't feel that the distribution -- the pattern of distribution precluded a benchmark analysis.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah, the discussions I had with U.S. EPA was, "Oh, you can't treat this like true continuous data, because it's categorical."

But I talked to several statisticians. And what I -- they don't know how else to treat it.

PANEL MEMBER BLANC: Right. Okay.

DPR ASSOCIATE TOXICOLOGIST LEWIS: And actually what I'm working with is the average store for each individual. And so by -- at that point to me it starts to become continuous data. But I don't know if Stan --

PANEL MEMBER BLANC: I think it may have more to do with the --

DPR ASSOCIATE TOXICOLOGIST LEWIS: -- just the distribution.

PANEL MEMBER BLANC: -- the cutoff that we use, you know, the 5 percent or so, if that makes sense in this -- whether that's conservative enough.

But I would say that the point -- the specific point of OEHHA, which I hadn't thought of before in terms of using ten instead of three for the NO effect, keeping with the .5, that might be somewhat more conservative. It doesn't give you a radically different answer but something that's -- it sounds like it comes out to 13. Or whatever it comes to, it will come to something like half of what you have now but not an order of magnitude change.

So that does sound like a reasonable response to that problem. And of course when you use the nasal nitric oxide, that's not normally distributed either, but it is a

measure where you have more confidence that the unit distance is the same. For me, the simplest form of the problem isn't that it's not a continuous variable. The problem is that you can't know that the distance between 0 and 1 is the same as between 1 and 2, is the same as between 2 and 3, even though you're telling people to rate your eye irritation on a scale of 0 to 5, because actually nobody said, for example, that -- well, some people might have said they had 5. But to go from 3 to 4 may be a bigger jump for someone in their interpretation. Whereas the nitric -- the nasal nitric oxide is more truly a unit --

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay.

PANEL MEMBER BLANC: -- difference.

CHAIRPERSON FROINES: Does OEHHA use .05?

PANEL MEMBER BLANC: They were fine with that. And we could hear from them later. Their question was whether or not once you got past that stage, whether the intraspecies question should be three or ten.

CHAIRPERSON FROINES: Well, I think this question of what number one chooses for the benchmark is an issue for discussion, not necessarily in this context but in general.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Generally we use a 5 percent response level unless there's -- it's

either less of a concern, you know, as -- and in the case of the eye irritation, we considered mild and reversible. Whereas most things we would use 5 percent unless we had greater concern. And you'll see later on we actually went down to 2.5 percent for --

PANEL MEMBER BLANC: -- bronchiectasis.

DPR ASSOCIATE TOXICOLOGIST LEWIS:

-- bronchiectasis. So --

PANEL MEMBER BLANC: By the way, to just follow up on John's point, I think that parenthetically what you should present in the text would be -- let's say you choose to go with a $BMCL_{05}$ for NO but with a tenfold adjustment. You can certainly present what the -- if you were to do the eye at 05 and only use a threefold, what that would look like. I think it would come out to be something quite similar probably arithmetically.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah, actually OEHHA did ask me informally what the $BMCL_{05}$ was for eye irritation. And if I recall, somewhere around 17 ppbs.

PANEL MEMBER BLANC: Okay. Thank you.

CHAIRPERSON FROINES: To be using -- because, you know, we've used the 95 percent upper confidence limit for the linearized multi-stage model since time began. And the question is -- we haven't debated some of these numbers very effectively in my view.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. Well, moving along.

Because of uncertainties about extrapolating the 1-hour NOEL out to evaluate 8-hour and 24-hour exposures, a rabbit developmental toxicity study was selected for estimating 8-hour and 24-hour NOELs. In this study pregnant rats were exposed 6 hours per day from gestation day 7 through 21. And the maternal effects that were seen in the first few days of exposure were considered acute. And these included deaths, discolored lungs, pulmonary edema, clinical signs of sensory and respiratory irritation, and reduced body weights and food consumption.

And I'll just go ahead and move on to this table.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: It's Table 12 in the document. And it's an abridged form of it because of space.

The incidence data in this table, the number outside the parentheses is the incidents between gestation days 7 and 11, in other words in the first five days of exposure. And then the number in the parentheses is the incidents after the first five days of exposure.

And you can see there were a number of deaths that occurred -- in fact, most of the deaths occurred early on in this study. And some of them had -- usually

the ones that were dying had other signs of respiratory and ocular irritation. Probably the most sensitive clinical sign was the nasal discharge. However, it didn't lend itself to benchmark dose analysis because of the non-monotonic dose response.

Most of the animals that died had red discolored lungs. Well, in fact, all of them had red discolored lungs. And then many of them also had edema in the lungs.

Some of the other more sensitive endpoints were reduction in the body weight gain during the first week and in the food consumption.

And one of the reasons I'm showing this data too is to show that there really isn't a lot going on at this dose level other than these late onset nasal discharge. And so I think that the lowest dose group -- or dose level in this study is really a NOEL, and a benchmark dose analysis is not needed for this.

So this study was then used to estimate 8-hour and 24-hour human equivalent concentrations, which came out to be 270 ppb and 92 ppb.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: And I'd also like to mention that OEHHA in their findings suggested that we use the 1-hour RfC for increased nitric oxide for evaluating the eight-hour exposure. Now they estimated

the one-hour RfC by dividing by an additional uncertainty factor of 3 for children. In our document, when we calculated the eight-hour RfC, we did not include an additional uncertainty factor of 3 for children. But if you did do that, then the eight-hour RfC from the rabbit study would still come out to be lower, at .9 ppb, than the one-hour RfC that OEHHA had estimated.

So I still think it's more health protective to use the eight-hour RfC derived from the rabbit study to evaluate those eight-hour exposures than using the one-hour RfC from the human study.

PANEL MEMBER BLANC: Presuming that you throw in the extra --

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah, assuming you're -- I think you need to be consistent, whatever you do, yeah.

PANEL MEMBER BLANC: Right, right. So you'd have the factor of 3.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Um-hmm.

PANEL MEMBER BLANC: And the endpoint that you're looking at, even though it was a developmental study, was the maternal health?

DPR ASSOCIATE TOXICOLOGIST LEWIS: The maternal effects, yes.

What fetal effects were seen were seen at the

higher dose levels, so they didn't come -- usually we assume any acute -- or any thiol effects that are seen in a developmental study are acute effects that could come from one day of exposure. But there weren't -- there wasn't a significant increase at the lowest dose level, so I didn't put it in that table.

PANEL MEMBER BLANC: Right. So therefore there was not a rationale for beyond the factor of 3 adding in an added multiplicative factor for major gaps in the database?

DPR ASSOCIATE TOXICOLOGIST LEWIS: The only -- I was going to discuss this later on. The only possible data gap was in the rat reproductive study. They did not expose the neonates directly from birth to day 28. So there is some potential increased sensitivity during that neonatal period. And that's --

PANEL MEMBER BLANC: So would that apply more to your 24-hour than your 8-hour level? Or what would that apply to, that uncertainty?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Well, I was -- I mean I'm just assuming you'd apply it across the board, but you may -- I think that one of the arguments that OEHHA had for using the uncertainty factor of 3 with one hour was there was also higher incidents of asthma among children, not just that there was this potential data gap

there.

But certainly if you're going to use it for one hour, it seems to me you should use it for --

PANEL MEMBER BLANC: No, no. No, I wasn't -- I support your use of addition of the three here. I was asking whether you needed to go farther than that. And it sounds like you don't believe that since the neonatal -- since the effects on the offspring that you saw here were only at higher doses and not at the lower doses, it doesn't sound like beyond the 3 there has to be yet another multiplicative factor.

DPR ASSOCIATE TOXICOLOGIST LEWIS: I would agree.

PANEL MEMBER BLANC: Is that what you're saying?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah.

CHAIRPERSON FROINES: Yeah, I got that same impression from your documents.

PANEL MEMBER BLANC: And this may be one thing that you want to say a little bit more explicitly. When you -- you're going to have to add in that you're now using this factor of 3. But you can say that you didn't feel that you needed to have a special added uncertainty factor.

CHAIRPERSON FROINES: Yeah, I think that's a good idea.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Now, I didn't

specifically mention a specific number in my document, because our department doesn't have a policy yet as to how we use additional uncertainty factor with children. And --

PANEL MEMBER BLANC: Again, this isn't related to -- I mean you're taking into account intraspecies variability with a factor of 3. What I was asking was in certain unique circumstances beyond -- up to 10 and then up to 10 again, which is a factor of 100 going from interspecies and intraspecies, there are times when we also throw in yet another multiplicative factor if we're concerned about a substance, one of whose major routes of toxicity appears to be teratogenicity or similar effects. And the database has such holes in it, that we don't seem to have any sense of developmental toxicity effects. But I think that in this case, a) we don't -- we don't suspect that that's the major route by which chloropicrin would be having its effects and b) there is already some data which didn't see something, so --

CHAIRPERSON FROINES: Why -- I have two questions for you. One is, why do you assume that that's not a major pathway for -- developmental effects aren't a major pathway?

PANEL MEMBER BLANC: Well, to the extent that, you know, that the data is out there, it hasn't seen it.

And then when you're thinking about substances which act primarily through acute injury effects, although we're going to be talking about carcinogenicity later, it just doesn't seem to be a dominant effect here or something, which it's not a neurotoxic metal, it's not a -- you know.

CHAIRPERSON FROINES: Yeah, but --

PANEL MEMBER BLANC: Just up on practice we --

CHAIRPERSON FROINES: The problem is, is that the data that we have, which goes back to World War I -- as she well knows, the data on other health endpoints and especially chronic or even subchronic, that data is -- we're making a conclusion based on less data than we would like to have.

PANEL MEMBER BLANC: I understand. It's just -- I'm just basing it on what has been our approach -- what is the precedent for our approach of invoking beyond the standard factors major data gap adjustments? And so far they haven't made an argument that suggests that we need to invoke that. And I think there --

CHAIRPERSON FROINES: Well, the --

PANEL MEMBER BLANC: I'm just basing it on what our precedent is up till now.

CHAIRPERSON FROINES: The certainty in the data is an issue which deserves consideration.

DPR ASSOCIATE TOXICOLOGIST LEWIS: I have another

slide later on discussing the potential pre- and postnatal sensitivity. I can talk about that more when I get to that if you'd like.

PANEL MEMBER BLANC: Okay.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: So that's all I have to say about the 8-hour and 24-hour NOELs that were derived in this document.

CHAIRPERSON FROINES: Let me ask you a question. Because this is -- this is a very important issue in some ways. Because the question is where we have -- if one used to say just a factor of 10 because of a lack of data, you would get a number. And she has the number using 3. And the question is, in the document should there be a policy that says, "Let's look at if we chose this, we would get this; and if we chose this, we would get this."?

And then you'd have some sense of the uncertainty that you're dealing with.

DPR ASSOCIATE TOXICOLOGIST LEWIS: We often do that in the risk appraisal sections. You know, in my document here I talk about alternatives for estimating the acute -- the benchmark dose from the human study. And we certainly could do a similar thing for this.

CHAIRPERSON FROINES: Well, Let's go ahead, because I think we've -- I think you're on target.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. With the subchronic studies available for chloropicrin, the lowest NOELs were seen in the 90-day inhalation toxicity studies with the rats and mice. These studies involved six-hour exposures per day, five days a week for 13 weeks. And effects were seen in both species at 1.03 ppb and higher, and included mortalities, clinical science reduced body weights, food consumption, increased lung weights, and a variety of pathological lesions in the nasal cavity and lungs.

PANEL MEMBER HAMMOND: Excuse me. Is that 1 ppb or 1 ppm?

DPR ASSOCIATE TOXICOLOGIST LEWIS: That's 1 ppm. Did I say ppb?

PANEL MEMBER HAMMOND: You did.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. Sorry.

PANEL MEMBER HAMMOND: It's 1 ppm?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah.

Because some of the respiratory lesions showed an increase at the lowest dose level, although often not statistically significant, a benchmark dose analysis was performed on the more sensitive endpoints. And with this analysis, a 5 percent response level was used because these were frank effects.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: This is a summary of the more sensitive endpoints seen in mice. This is from tables 3 and 4 in the document. And the more sensitive endpoints in the mice were the epithelial highland inclusions and rhinitis in the nasal cavity and alveolar histiocytosis in the lungs.

And you can see that generally the females had a higher incidence than the males, although not dramatic.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: In rats, slightly different. Respiratory lesions appeared to be the more sensitive endpoints. Besides rhinitis, they also saw an increase in goblet cell hyperplasia, peribronchial and peribronchiolar muscle hyperplasia, and bronchial and bronchiolar epithelial hyperplasia.

A benchmark dose analysis was not done for the goblet cell hyperplasia even though there was a significant increase at the lowest dose level. And this was because the dose response in the females was non-monotonic and I couldn't get a good fit with this data.

And also in males, the increase was not significant by either trend or pairwise degrees.

PANEL MEMBER HAMMOND: Well, wait a minute. There was no -- there was a large effect. Seventy percent

were affected at no dose.

DPR ASSOCIATE TOXICOLOGIST LEWIS: In the males?

PANEL MEMBER GLANTZ: The lowest dose -- or no dose.

PANEL MEMBER BLANC: No dose.

PANEL MEMBER HAMMOND: But the no dose you've got seven out of ten affected.

PANEL MEMBER BLANC: Well, it's not an effect if there's no exposure, is what she's trying to say.

PANEL MEMBER HAMMOND: Yes. But it's not that there's -- there's a difference between a lack of adults response curve and a lack of an ability to see it. You wouldn't be able to see a dose response curve in this case.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah.

PANEL MEMBER LANDOLPH: The background's too high.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah, the background's too high.

PANEL MEMBER HAMMOND: Yeah, the background's too high.

So it's not that there's no dose response. We can't tell.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah, I guess I just -- yeah, it didn't --

PANEL MEMBER HAMMOND: There was a difference.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. I see your point. Okay.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: So Table --

CHAIRPERSON FROINES: That thing is very interesting when you think about it, because the females, the data is quite strong.

PANEL MEMBER BLANC: Well, we'll come back to that when we come to cancer maybe. But, anyway.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. So this is a summary of the benchmark dose analysis performed on these more sensitive endpoints. And the lowest $BMCL_{05}$'s were seen in mice for -- in females for epithelial highland inclusions and alveolar histiocytosis. However, when we converted these to human equivalent concentration, taking species' differences in breathing rate into account, actually the female rats had the lowest ATC for rhinitis. And so this ATC was used to evaluate the subchronic or seasonal exposures to chloropicrin.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: A similar situation occurred in the chronic toxicity studies. The lowest NOELs were seen in the inhalation studies in both rats and mice. And mice, however, were only exposed for

78 weeks. The rats were exposed for 107 weeks. The LOEL -- apparent LOEL in these studies was the same, but .5 ppm in both species. However, the effects were more severe in mice, with numerous respiratory lesions, whereas the rats, the only respiratory lesion seen was rhinitis.

And I'll show you the incidence of these.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: These again are just the more sensitive endpoints that were seen. And in mice, the lesions were the same. Essentially the more sensitive ones were the same as that seen in the subchronic study, with the exception of bronchiectasis, where there was a dramatic dose-related increase in this effect.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: And again in rats, the only thing seen was the increase in rhinitis, primarily in the males.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: So this is a benchmark -- the summary of the benchmark dose analysis performed for the more sensitive endpoints. And initially a 5 percent response level was used with all of these. However, Dr. Blanc suggested that we reduce the response level for the bronchiectasis down to 2.5 percent because

of the irreversible nature of this lesion. So I have here in parentheses the $BMCL_{05}$, and then on top there is the BMCL at 2.5 percent response level.

Yes.

PANEL MEMBER HAMMOND: In many of these endpoints you've been talking about, there were what appear to me - and it's not my field - to be fairly high levels of outcomes in the control groups. And to that degree, that's always going to limit your ability to detect and define effects. And I don't know whether that -- how that relates to historical, other control groups and other studies.

Have you looked at that at all?

DPR ASSOCIATE TOXICOLOGIST LEWIS: I did not look at that.

PANEL MEMBER HAMMOND: I mean so I think it's of some importance whether these control animals had higher rates of these things or whether that's the normal background levels.

DPR ASSOCIATE TOXICOLOGIST LEWIS: So you're wondering if there's, you know, current disease or something as that?

PANEL MEMBER HAMMOND: You know, and go back like -- I mean, look at my -- I don't know anything about the health of rats generally in labs. But some of these

things seem to have relatively high levels in the control group to me. But --

PANEL MEMBER BLANC: Well, I think that would -- I'd be more concerned about that if it was so true across the board that they couldn't analyze anything. But since they do have some endpoints that are good -- are solid endpoints and that some of the things for which there were pretty high rates and the control groups are less pathological anyway, like a little bit of rhinitis, I'm not so concerned that that limits their ability.

But one question that I would have since one thing that drives your benchmark calculations mathematically is the noise of the system --

PANEL MEMBER HAMMOND: Yeah, basically contributes to that.

PANEL MEMBER BLANC: Yeah. So it's nice the one that you've chosen, the bronchiectasis, doesn't have any observations in the referent group. But --

DPR ASSOCIATE TOXICOLOGIST LEWIS: It also has a very high -- or the highest incidence at the high dose.

PANEL MEMBER BLANC: Right. Yeah, so it's monotonic.

Would you have more security in your estimate if you combined the observations in the males and females since they are almost identical? Would that change

your --

I can look at that. When we do that, I always tend to keep the sexes separate.

PANEL MEMBER BLANC: I know. But in this particular case they're so very close.

DPR ASSOCIATE TOXICOLOGIST LEWIS: You know what I think it would do -- let me move. Actually though I think it would increase the BMCL. Because if you look at the males, you're coming out with a higher estimate. So if you average this data, I would think that this would actually bring the BMCL up.

PANEL MEMBER BLANC: But it would give you more security in the estimate, wouldn't it?

DPR ASSOCIATE TOXICOLOGIST LEWIS: That would --

PANEL MEMBER BLANC: I don't think it's going to bring it up very much.

DPR ASSOCIATE TOXICOLOGIST LEWIS: No, it's not dramatic, four eighteen and fifty.

CHAIRPERSON FROINES: Why don't you take a look at it.

PANEL MEMBER BLANC: Because it's nice -- you know, bronchiectasis is a hard endpoint.

PANEL MEMBER BYUS: What is it exactly? Since we're talking about it. Refresh our memory as to what exactly it is.

PANEL MEMBER BLANC: It's pathological changes in the airways where they're erratic and violated.

PANEL MEMBER HAMMOND: They're what?

PANEL MEMBER BLANC: Erratic and dilated. And so it is associated with considerable morbidity in humans when you have this problem. It's a sequela of irritant damage. It's also an after-effect of bad infection. But, for example, in the --

PANEL MEMBER BYUS: Is it irreversible?

PANEL MEMBER BLANC: Yeah, it's irreversible.

PANEL MEMBER BYUS: That's the key thing.

PANEL MEMBER BLANC: And it can be progressive, because it tends to lead to a cycle of chronic infection and then worsening. And there's good precedent for this to be an after-effect of an irritant. It's certainly been shown in human irritant inhalation injury that you can get bronchiectasis. And I think that's best shown in the Iranian survivors of Iraqi mustard gas attacks.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. If the discussion's ended with that, I'll move on to the carcinogenicity.

In the weight of evidence for carcinogenicity, the genotoxicity studies were evaluated. And there are a number of positive tests. The most notable were all eight

reversed mutation assays with salmonella were positive usually with TA100 with activation.

Also notable was a positive Comet assay with TK6 cells that show high levels of primary DNA damage. Other notable positive assays was an in vitro chromosomal aberrations assay with CHO cells and a cystochromatid exchange assay with human lymphocytes.

There were also notable negative assays, including a forward mutation assay with mouse lymphoma cells in vitro and in vivo micronucleus assays and in vitro chromosomal aberrations assay with human lymphocytes.

However, due to the positive task for gene mutation in DNA damage, DPR concluded that a genotoxic mode of action for tumor formation was possible.

--o0o--

CHAIRPERSON FROINES: I think when you take into account the electrophilicity of the compound, that adds to the weight of the genotoxicity outcomes.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. In the carcinogenicity studies for chloropicrin, an increase in lung tumors was seen in one inhalation study with mice. The increase was significant for adenoma -- well, let me just move on to the next slide.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. And this table summarizes the lung tumors in female mice seen with the inhalation carcinogenicity study. And there was -- oh, and I should point out the denominator in the first three rows is the number of animals that survived today, 253, which was the time the first tumor was observed -- the lung tumor was observed.

And when expressed -- the incidence was expressed this way, there was a significant trend in the incidence of the adenomas as well as the combined incidence of adenomas and carcinomas. However, there was not a significant increase in pairwise comparison. Although I have to point out that when the incidence was combined for adenoma and carcinoma, the Fishers exact test approached significance level with a P value equal to .053.

CHAIRPERSON FROINES: Can I make one comment?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah.

CHAIRPERSON FROINES: Unless I'm mistaken -- well, I'm not mistaken -- this is a 78-week study instead of 104 weeks, which is what we'd prefer. And so when you're comparing 78 weeks, you're dealing with a very -- with a relatively young animal compared to the chronic animal bioassays that the NTP does, which are 104. So you're not going to expect to see cancers at 78 weeks. You would expect to see cancers as the animals

reach -- you know how the curve goes. We all know how the curve goes. And 78 weeks makes these studies -- the fact that you're finding positive results is striking given the age of the animals, I think.

PANEL MEMBER LANDOLPH: Yeah. And I would add to your comment -- I was looking at the carcinoma data again. It's positive. It's not terribly dose responsive at this point. That may be because of the consideration you just raised. It also may be because the dosing -- you know, maybe you should extend it higher and lower. But that's positive data.

And the adenoma data is positive against the high background. That background is very high.

So that's kind of the best you can do. But it is positive. I wouldn't say it's negative data.

DPR ASSOCIATE TOXICOLOGIST LEWIS: NTP recommends adjusting the tumor incidence based on survival even when survival is -- there is no dose-related effect on survival, which was the case in this study. And so we did a Poly-3 -- reexamined the tumor incidence using a Poly-3 trend test, which takes survival into consideration.

And one of the advantages of this trend test over some others that also adjust for survival is it doesn't require you knowing whether or not the tumor was the cause of death.

I should also note that the Poly-3 trend test is the default trend test that NTP uses.

With this test, the animals at risk, the denominator, are adjusted waiting the animals -- based on when they died and whether or not they had a tumor.

So the incidence in the bottom row here is the incidence calculated with a Poly-3 trend test. And you can see the numerator hasn't changed. It's just the denominator, the animals at risk, has changed.

And so with this analysis, not only is the trend significant. The incidence now at the high dose level comes out significant by pairwise comparison at the .05 level.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: There was an increase in tumor seen in another study. This was in an oral study in rats. There was a significant increase in mammary fibroadenomas in female rats that was significant by trend analysis and pairwise comparison.

DPR concluded that the weight of evidence was sufficient to warrant a quantitative assessment of carcinogenicity because there was a significant increase in tumors seen in two different species from two different laboratories and there was evidence of genotoxicity.

The cancer potency was then estimated to be

2.5 -- 2.3 per milligram/kilogram-day based on the incidence of the lung tumors in female mice.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: So this table just summarizes the critical endpoints and human equivalent concentrations that DPR used in their risk assessment for chloropicrin.

CHAIRPERSON FROINES: I was impressed with your table where you compared a whole range of compounds. And for this committee to have this compound be more potent than diesel is like our history being repeated for it again.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Well, it was interesting. It bothered me. I kept recalculating the cancer potency, because I didn't believe that number either, because that's been the highest potency factor I have ever calculate. But I think it's because the concentrations in the study are so low because of its high toxicity. That's why its potency is so high.

PANEL MEMBER LANDOLPH: And, in fact, I loved that Table 18. And when you read it according to your calculated potencies there, chloropicrin is equivalent to benzpyrene, dibenzo[a,e]-pyrene, 7H-dibenzo[c,g]carbazole, 1,8-dinitropyrene and 5-methylchrysene, and certainly benzo[a]pyrene and dibenzo[a,e]-pyrene and carbazole are

considered very strong carcinogens. So your number, 3.9, is equivalent to those.

So Dr. Errol Zeiger's arguments may be true that the mutagenicity, although positive, is weak. But the carcinogenicity certainly is not weak for this compound. It's very strong.

In fact, it's stronger than nickel, which is -- and they're known human carcinogens.

DPR ASSOCIATE TOXICOLOGIST LEWIS: I think one of the problems with demonstrating the carcinogenicity is because of its toxicity, that it's very hard to give it a dose level that doesn't end up killing it. So you have to do a delicate balance in order to show the --

PANEL MEMBER LANDOLPH: And it often occurs with things like MNNG as an example, which is causing horrendous killing while it's causing mutagenesis and carcinogenesis. And this is similar.

CHAIRPERSON FROINES: We were impressed with the Chromium 4 that was so potent.

(Laughter.)

CHAIRPERSON FROINES: Do you have that in front of you?

DPR ASSOCIATE TOXICOLOGIST LEWIS: No, no, I don't.

CHAIRPERSON FROINES: Joe, does, I think. And

Kathy does.

PANEL MEMBER LANDOLPH: They meant Chromium 6. It's a transportation --

DPR ASSOCIATE TOXICOLOGIST LEWIS: Oh, yeah. Okay, yeah.

PANEL MEMBER BYUS: Yeah, I'd like to just comment since we're -- just about a minute about the carcinogenicity as well. I mean I think that you're right about the toxicity. But I think more specifically - and you mentioned it in here - it's the lack of weight gain and the caloric restriction that could be even more vastly underestimating this. And so these animals, and you have the data throughout that says this, are not gaining weight and they're not -- most of them aren't eating as much food. So it winds up being nutrient as well as caloric restriction. And so what that will do is vastly underestimate the number of tumors that you're going to see in your experimental group versus your control group.

And I really worry about this a lot with a lot of toxic, even semi-toxic compounds. So I mean I think -- that's all.

PANEL MEMBER LANDOLPH: And, you know, to continue that argument, I think this is the tip of the iceberg, because I loved your table on page 2 where you're calculating RfC's for children and adults, and they're,

you know, .73 to 8.7 parts per billion. And then if you use a default presumptive linearized dose response curve for this as a carcinogen, you come up with .23 parts per trillion, i.e., four orders of magnitude lower. So at some time when it's appropriate, I'd like to still open a debate as to how we recommend this be regulated.

CHAIRPERSON FROINES: Well, I think that the point is that when you add in -- what you've just said, you add in the nutritional issues, you add in the 78 weeks, and you add in the electrophilicity of the compound, you have -- you've really added more, much more weight to the conclusion than you had before in some respects. And so it's useful to add that and it's -- because you've done such a good job up to this point.

PANEL MEMBER BLANC: Can I just clarify those.

The values that are in the second column actually are going to change downward for several of those based on what we've been discussing so far?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Well, those are the ATCs too. Those aren't the reference concentrations. So they don't have all the uncertainty factors applied in there.

PANEL MEMBER BLANC: I see.

DPR ASSOCIATE TOXICOLOGIST LEWIS: So there's no additional uncertainty factor for children. The HEC for

the one hour actually would go up because I'm using the nitric oxide increase. But then the RfC would go down because of larger uncertainty factors applied to that.

PANEL MEMBER BLANC: Right. And is there -- where does this table appear? This is the --

DPR ASSOCIATE TOXICOLOGIST LEWIS: It's page 59 I have up there. I tried to --

PANEL MEMBER BLANC: Right. And so that one we can see actually the RfC in that table as opposed to this one?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah, I just -- you know, with space limitations I just --

PANEL MEMBER BLANC: No, no, no, no, no. I just want -- what I wanted to do was make sure that the values, as opposed to this one where there are some -- the values are higher for certain categories, even though it's a longer exposure -- but actually when you do the RfC, it's --

DPR ASSOCIATE TOXICOLOGIST LEWIS: Yeah, that's deceptive when you look at the human study compared to the animal study.

PANEL MEMBER BLANC: Right, I gotcha. Okay.

PANEL MEMBER FRIEDMAN: I'd like to ask Craig, could you explain the mechanism you're referring -- is it that the bad nutrition shortens their life or is it that

it --

PANEL MEMBER BYUS: The most accepted, any animal model for cancer, and even human model -- human model -- but even in humans now and chimpanzees and primates, the most effective thing you can do to prevent cancer in a carcinogenicity cancer model like a non-transplantable is to restrict calories, as opposed to restricting nutrients. Simply a caloric -- nutrient -- obviously if you reduced the vitamins, things like that, that also can increase your -- or reduce your incidence. But if you actually just reduce the calories below a certain -- I mean they've calculated how much this is. It has to do with ad libitum-fed diets for animals versus what they would get in the wild, for example. And for human beings, we're talking about being a very hungry person, okay, if you were going to -- to get down below caloric -- we're not just talking about being thin. We're talking about being sort of uncomfortably hungry and slightly underweight. But you markedly increase life span and you markedly reduce the tumor incidence.

And so for animal studies, you have to be very careful that the animals are -- all have the same weight and et cetera when you do these comparisons. And for many classic carcinogens that just affect DNA that aren't necessarily so innately toxic, if you put those animals on

a caloric restricted diet, you markedly reduce the tumor incidence.

So in these kinds of studies where you're giving nasty tasting, smelly things, that ultimately reduce the body weight, that's going to undoubtedly reduce the tumor incidence.

CHAIRPERSON FROINES: But I would --

PANEL MEMBER BYUS: I mean that's in a nutshell what it is. And, again, this state has progressed enormously now, because now they've identified some of the genes that are involved. In primates they've done these studies. They didn't know whether this worked in primates. They do now know that the same thing happens in primates as it does in rodents. And they've actually now identified some of the genes that they think are involved in this.

So I mean the mechanism is beginning to be actually worked out molecularly.

CHAIRPERSON FROINES: It's actually a little bit more complicated.

PANEL MEMBER BYUS: It is.

CHAIRPERSON FROINES: Because I did a two -- I did a chronic animal bioassay with arsenic. And we -- the animals were deficient in choline, folic acid, and creatinine. And we produced enormous numbers of cancers

in the animals with no arsenic. And so their nutrition is another factor.

PANEL MEMBER BYUS: Correct. And when I talk about the caloric restriction alone, that they control for the nutritional variability in a classic experiment. But some of the older, quote, caloric restriction experiments wound up being nutrient restricted as well as caloric restricted.

So what you have to do as animals wind up eating, you have to make sure you have the same exact levels of nutrients in your diet. So you have to modify the diet formulation in order to make sure the animals in every group get exactly the same amount of nutrients as well as being reduced in calories in a dose responsive manner. So

See what I mean?

PANEL MEMBER FRIEDMAN: So you need calories to form a tumor?

PANEL MEMBER BYUS: Well, it's probably more -- that's simplistically. But molecularly now -- and I wish I could remember the gene that they've identified. They've identified a number of genes that they think are mediating this.

CHAIRPERSON FROINES: We should move ahead, because this could turn into a whole discussion because it's so topical.

PANEL MEMBER BYUS: You did in your document present this and you discussed it in a sense probably not as I would be able --

DPR ASSOCIATE TOXICOLOGIST LEWIS: No, as at length as you have.

PANEL MEMBER BYUS: Right. But you did present that in there and you do mention the fact that these animals are losing weight, et cetera.

PANEL MEMBER FRIEDMAN: Well, the manufacturers have apparently questioned the carcinogenicity. So anything that you can --

PANEL MEMBER BYUS: Well, as John said -- I think John's little summary of the three or four -- the four additional things that we would all believe would add to the weight of evidence I think is very persuasive. I'd like to see that enumerated somewhere. Joe's --

PANEL MEMBER LANDOLPH: And you can question -- anybody can question carcinogenicity. But if it's up around benzopyrene and it's higher than nickel, which is a known strong human carcinogen, I don't agree with them.

PANEL MEMBER FRIEDMAN: Well, they have some, quote, expert statisticians saying that the tests that were done were not appropriate or whatever. I just think that that should be dealt with fully.

PANEL MEMBER LANDOLPH: Yeah. My opinion is you

have to be careful when you look at this -- you know, this data. Obviously these are not the perfect animal assays. But I would find it difficult to make this data go away from in front of my eyes. I think there's too much of it, number one. And, number two, when you're getting potencies above nickel and around diesel exhaust and benzopyrene, that's very difficult for me to make it go away. So I don't agree with that. I see their arguments, but I don't agree.

CHAIRPERSON FROINES: In terms of my points, Gary, a 78-week assay is an incomplete study.

PANEL MEMBER FRIEDMAN: I'm not trying to defend the manufacturer's position. I'm just saying it's out there and it should be dealt with.

CHAIRPERSON FROINES: And then when you add the electrophilicity of the compound, it reinforces her perception of the data. It just adds to the weight of the data.

PANEL MEMBER GLANTZ: Well, I think what Gary's saying, he's agreeing with you. I think he's just saying -- I think everybody's saying you just want to have this all pulled together in one place, maybe even a little table that says, you know, here are several important -- you know, when you look at the biases that are built into the studies, they're all biased against finding a result.

PANEL MEMBER HAMMOND: Yeah, exactly.

PANEL MEMBER GLANTZ: And yet you still got the result.

PANEL MEMBER BYUS: Correct.

CHAIRPERSON FROINES: Just for her benefit, I did a 16-week study, and I've never recovered from how badly that was designed. So I say what I say with just self -- with some humility.

PANEL MEMBER GLANTZ: Why don't we go on.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. Moving on.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. So to evaluate the risk for non-carcinogenic effects a margin of exposure was calculated, which is the human equivalent concentration divided by the air concentration either from air monitoring or air modeling. And generally an MOE greater than a hundred is desired, assuming that humans are ten times more sensitive than animals and that there's a tenfold variation in the sensitivity of the human population.

In order to not list a pesticide as a toxic air contaminant, however, the MOE needs to be tenfold lower -- the air concentration needs to be tenfold lower than those that are considered protective of human health.

This translates into the MOE being greater than a thousand.

However, for sensory irritation, the MOE only needed to be greater than 30 because there was no interspecies uncertainty factor for this endpoints till it's based on a human study. Also, the intraspecies uncertainty factor was reduced to 3 because no toxicokinetic variation was expected due to its direct acting mechanism of toxicity.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: For carcinogenicity, the risk was calculated by multiplying the potency times the exposure expressed in milligram per kilogram-day.

Generally a risk less than 1 in a million or 10 to the minus 6 is considered negligible. However, in order to not list a pesticide as a TAC, the risk needs to be less than 1 in 10 million

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. So these are the margins of exposure for bystanders of soil fumigation, assuming the worst exposure estimates. And you can see that they are well below the target MOEs of 30 and a thousand by several orders of magnitude.

(Laughter.)

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Even if you assumed the 50th percentile for application rate and field size, the margin of exposure for bystanders of soil fumigation were still well below the target MOEs.

PANEL MEMBER GLANTZ: But that's an understatement.

PANEL MEMBER HAMMOND: Well, you know, I would point out this is the material that is being used in California today. It's in use. There are people being exposed today. And these are health effects we're talking about that are happening. It's not -- I mean it's pretty astounding and overwhelming. But it's also -- this is real.

CHAIRPERSON FROINES: It also shows you why they used it in World War I.

(Laughter.)

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Even if you then had the bystander standing a half mile from the field edge and the application rate at the 50th percentile and field size of the 50th percentile, the margins of exposures are still below the target MOEs for TAC listing.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: This table

shows the risk estimates -- cancer risk estimates. And I only have the estimates for the application method that had the highest lifetime exposure estimates, which was the bed and tarp application method. And the risk estimates come out to between two and six excess cancer cases in a hundred people.

PANEL MEMBER HAMMOND: Excuse me. That's for the residential.

But the occupational, that's going to be the bystanders.

DPR ASSOCIATE TOXICOLOGIST LEWIS: That's the bystanders. The bystander can be residential or --

PANEL MEMBER HAMMOND: Right. But do you have an occupational number there?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Oh, I'm sorry. I have not even been paying attention to my own table.

Okay. This is -- yeah, this occupational -- these could be occupational.

PANEL MEMBER HAMMOND: No, but the occupational exposures haven't been estimated yet, right?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Oh, no. These are occupational bystanders as opposed to --

PANEL MEMBER HAMMOND: Exactly. And I think it's very -- no, but I think it's very important to put that word in there.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Oh, in the title.

PANEL MEMBER HAMMOND: In the title, because there's already in the previous, you know, presentation that we haven't even begun to look at the exposure of the people who are doing the application. This is the bystander --

PANEL MEMBER LANDOLPH: And this again --

PANEL MEMBER HAMMOND: -- occupational bystander.

CHAIRPERSON FROINES: Do we -- you will do occupational; is that correct?

PANEL MEMBER BLANC: Not for this process.

CHAIRPERSON FROINES: Yes. Because when the procedure for risk assessment changed a few years ago, occupation became one of the things that was added, I think -- I believe. That's correct?

So I guess we will see what Kathy is looking for.

PANEL MEMBER HAMMOND: Well, I mean I don't know whether -- you said that's several months away, right?

PANEL MEMBER GLANTZ: Well, I think all Kathy -- but it is in the title to the table. For her part she's right, it would be clearer if you said residential bystander and occupational bystander.

PANEL MEMBER HAMMOND: It's really important.

PANEL MEMBER BYUS: Right, it's confusing.

PANEL MEMBER LANDOLPH: And if I understand this table correctly, these are really quite stunning figures, because if you want --

DPR ASSOCIATE TOXICOLOGIST LEWIS: Oh, yes. I mean when your risk level is that --

PANEL MEMBER LANDOLPH: -- if you want it to be 10 to the minus 7, this is 100,000 fold higher than it should be. Even if it's de minimis, which is 10 to the minus 6, it's still, you know, 50,000 fold times higher. So this is why I'm -- with the potency, I certainly recommend that you give some more thought to this, please, and in terms of regulating this based on carcinogenicity, which would drive the levels down significantly lower.

PANEL MEMBER HAMMOND: And one other issue, and I don't remember the numbers. I just remember that the levels inside homes when people go back into their homes, after they've been fumigated and after aeration, they're still pretty high.

And it might be worthwhile putting those numbers in, because those are actually -- I don't know where they're going to fit into this, but I --

DPR ASSOCIATE TOXICOLOGIST LEWIS: There were no cancer risk calculations for the structural fumigation because there was assumed to be no chronic -- seasonal chronic or lifetime exposure since it would happen so

infrequently. So all we have are --

PANEL MEMBER HAMMOND: Right, I got you.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. So these are the MOEs for bystanders of structural fumigation. As you can see, they're higher than what we saw with soil fumigation. However, they're still below the target MOEs of 30 and a thousand.

PANEL MEMBER HAMMOND: And just, you know -- when she's using these terms, MOE, that's margin of exposure. And if you're at 1, you're already being exposed to the level where health effects are expected.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Well, it's equivalent to the no-effect level in an animal study.

PANEL MEMBER HAMMOND: Right, right. So I mean 1 is a problem. Anything less -- I mean of course we have targets and we do need the targets. We need to be there. But it's really quite a bit of concern I think when you're there.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: And this table summarizes the margins of exposures for indoor air associated with structural fumigation. This is after the aeration period. And they are lower than what you see for bystanders and therefore obviously of some concern.

--o0o--

CHAIRPERSON FROINES: Can I -- I just want to -- I was walking out when you were having that discussion about occupation. And I wanted to make sure everybody's clear. There is no legal responsibility under AB 1807 to address occupational issues. Occupational issues are -- I don't know law number, but they -- she'll do -- she will do occupation but not because of this TAC process.

PANEL LIAISON BEHRMANN: That's right.

PANEL MEMBER BLANC: Except for the occupational bystander.

CHAIRPERSON FROINES: Yes.

PANEL MEMBER GLANTZ: Well, let's move along.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Moving on. Okay.

These are the MOEs for bystanders of enclosed space fumigation. And these are almost the same as those you see with soil fumigation. They're quite low, and orders of magnitude less than the target MOE.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: And these are the cancer risk assessment -- risk estimated for enclosed space fumigation. And they are also quite low.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: This table compares the RfC's, the DPR calculated versus U.S. EPA. And I -- because of space limitations, I didn't include all the acute RfC's, the DPR calculated, because we had 1 hour, 8 hour, and 24 hour. I only included the 1-hour one from DPR, because it used the same endpoint that U.S. EPA used to evaluate 4-hour and up to 24-hour exposures.

And I mentioned earlier, they use a different approach for estimating the threshold in their benchmark dose analysis. So their BMCL came out much higher. And then they divided by uncertainty factor of 1 to come up with a reference concentration. So their reference concentration is the same as their BMCL value, whereas we divided the BMCL by 3.

With seasonal RfC's the same rat and mice inhalation studies were used, the differences being they identified the lowest dose level as a NOEL, whereas we did a benchmark dose analysis. However, when they converted the NOEL to a human equivalent concentration, they did an RGR adjustment for extra-thoracic effects. And then in doing that, they -- because that took some species differences into consideration, reduced the intraspecies uncertainty factor down from 10 to 3. So they used a total uncertainty factor of 30 in their -- when adjusting

from the ATC to the reference concentration.

We did not -- in ours we did a benchmark dose analysis. We convert to human equivalent concentrations. We do not do the RGDR adjustment. And instead we prefer to just use the standard default uncertainty factors of 100 to come up with our reference calculations. And this -- a similar thing happened with the chronic reference concentration.

The thing that's interesting is, given the differences in the approach, that we ended up with similar reference concentrations.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. I have just a couple other issues that I will mention before I finish here.

We did evaluate the potential for pre- and postnatal sensitivity to chloropicrin. And in the developmental toxicity studies in rats and rabbits, the fetal NOELs were always equal or greater than the maternal NOELs. Furthermore, the fetal effects that were seen were nonspecific signs, possibly secondary to the maternal toxicity.

In the rat reproductive toxicity study the pup NOEL was also equal or greater than the parental NOEL.

These findings to me are not that surprising

given how reactive chloropicrin is. I suspect probably significant amounts of chloropicrin don't enter the maternal bloodstream. So to me it's not surprising.

However, there is what you might consider a data gap in the rat reproductive toxicity study. It's not required by guidelines, but the neonates were not exposed directly to chloropicrin from birth to postnatal day 28. And they could be more susceptible to inhalation exposure chloropicrin because of the immaturity of the respiratory system, their immune system, and metabolic enzymes.

So an additional uncertainty factor for children may be appropriate.

Potential for endocrine effects was also considered. And the only things that appeared to be possible endocrine effects were some reproductive effects. But it's not even clear that these were endocrine related. They were fairly nonspecific effects and included reduced number of implantation sites, increased pre- and post-implantation losses and late-term abortions.

--o0o--

DPR ASSOCIATE TOXICOLOGIST LEWIS: So in conclusion, with soil fumigation --

CHAIRPERSON FROINES: Before you go on, is there any -- is there any literature on thyroid effects?

DPR ASSOCIATE TOXICOLOGIST LEWIS: I'm not aware

of any, no.

CHAIRPERSON FROINES: Thanks.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay. So in conclusion, with soil fumigation, all the bystander MOEs are significantly less than their target MOEs, as well as the cancer risks being significantly greater than their target risk levels. So clearly the off-site air concentrations associated with soil fumigation meet the criteria for listing chloropicrin as a Toxic Air Contaminant.

With structural fumigation, all the bystander MOEs were significantly less than their target. Also the MOEs for indoor air were significantly less than their targets. And so the off-site and indoor air concentrations associated with structural fumigation also meet the criteria for listing chloropicrin as a toxic air contamination.

And with enclosed space fumigation, again the bystander MOEs are significantly less than their target MOEs and the cancer risks are significantly greater than their target risk levels. And so the off-site air concentration associated with this use clearly meet the criteria for listing as a TAC.

So that concludes my presentation. Are there any more questions?

CHAIRPERSON FROINES: I think everybody on this panel would agree that that was an extremely fine presentation, and we appreciate it very much.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Thank you.

CHAIRPERSON FROINES: That was really terrific. And your slides themselves were very easy to read and understand. So it makes a big difference.

So we have -- Paul leaves in 25 minutes. And the question is -- we can start going through the panel with any questions and -- the question, Peter, I don't know, is, in terms of people's flights --

MR. MATHEWS: We could go till 2.

CHAIRPERSON FROINES: No, but can we go after 2 if Paul leaves?

MR. MATHEWS: Yes. To a certain extent, yes.

PANEL MEMBER BYUS: Not really.

CHAIRPERSON FROINES: I personally would like Paul -- Paul was the lead. And so --

PANEL MEMBER BLANC: Co-lead.

CHAIRPERSON FROINES: Co-lead. Sorry.

PANEL MEMBER GLANTZ: Well, why don't we just see what questions people have?

CHAIRPERSON FROINES: We will. But I want to make sure that if -- I want to just ask the question, that when Paul leaves, do people want to stop or continue later

in the day?

PANEL MEMBER LANDOLPH: Well, Peter, could you get us later flights out? I don't mind hanging around to finish business.

MR. MATHEWS: It's doable, but I can't be certain.

PANEL MEMBER BYUS: No, I'm leaving at 2 as well.

CHAIRPERSON FROINES: Oh, you are?

PANEL MEMBER BYUS: I have to, yeah. My flight's -- I've got to get out of there. I don't think there is another flight for me. So I have to get out.

CHAIRPERSON FROINES: So then I would say, unless somebody strongly disagrees, that we close the meeting at 2 o'clock.

And that during the time between this meeting and next meeting, the leads work on the findings. And we can bring this to closure at the next meeting.

PANEL MEMBER GLANTZ: Yeah, I think that's probably true. Why don't we see what remaining questions people have in the next half hour.

CHAIRPERSON FROINES: Okay. Paul, why don't you start -- well, Kathy, why don't you start, because you worked with one of the co-leads.

PANEL MEMBER HAMMOND: Well, I was. But since Paul -- oh, we're going to stop anyway at 2, right? Okay.

I haven't sat there and looked at this directly. But remembering that chloropicrin is used both as an active ingredient and as a warning agent, to what degree do these findings hold when chloropicrin is used as a warning agent at the less than 2 percent -- say at the 2 percent or 1 percent level?

DPR ASSOCIATE TOXICOLOGIST LEWIS: Well, I mean the only thing we've done where it's just used as a warning agent is the structural fumigation studies. But if you look at the soil fumigation, it's a dose-related effect. So you would obviously have to, you know, reduce -- yeah, reduce --

PANEL MEMBER HAMMOND: Well, yeah. I guess what I'm saying is I think it might be worthwhile to fold into -- to make tables to fold in, tables that include what's the MOE when it's used as a warning agent.

DPR ASSOCIATE TOXICOLOGIST LEWIS: So, say, with soil fumigation, say --

PANEL MEMBER HAMMOND: Right.

DPR ASSOCIATE TOXICOLOGIST LEWIS: Okay.

PANEL MEMBER HAMMOND: I mean I think -- you can do this, right?

DR. BEAUVAIS: Certainly it can be done. I mean basically what we're assuming, we'd just say, you know, 2 two percent of the exposure. And then they're going

to -- yeah, that's...

The reason that we haven't been doing that, for example, for lifetime exposures is that it's really difficult with multiple exposures to assume that somebody would only be exposed to a particular concentration. And so that's where we end up saying, "Okay, what's the reasonable worst case?" And that's really what we're looking at here. I mean we can go away from the screening estimate approach. But -- I guess in terms of what the intent of this document is.

Now, when we get to the full exposure assessment, there actually -- the occupational breaks out that way, is a hundred percent chloropicrin and then the 10 1/2 percent chloropicrin for that one single product, and then 2 percent chloropicrin for warning agent products. So the occupational in the full exposure assessment looks at it that way because it makes sense, because it's feasible that somebody could go on repeatedly. You know, if you're working on a crew that this is -- you know, they use a methyl bromide product all the time, this is what they do, then that makes sense.

But I guess in terms of screening estimates for bystanders, I'm not sure that there's a lot of value in looking just at the warning agent use when we have these active ingredient uses also.

PANEL MEMBER HAMMOND: Well, I guess what --

MS. BEAUVAIS: Because again the question that we're attempting to answer here is, does this meet the criteria for listing as a toxic air contaminant?

PANEL MEMBER HAMMOND: And I guess -- and I may be anticipating. I may be -- john, you can correct me if I'm going where I shouldn't go. But I'm wondering with -- you know, it looks here like a lot of excellent evidence between the two of you and all the people behind you who have been doing all this work, you know. And I think both of you've done wonderful jobs in the presentations. You made a very strong case, you know, that the margin of exposure is like beyond belief.

But if one removed chloropicrin as an active ingredient, the question -- would we be in a situation where we would have to come back and revisit this as a warning agent? I'm just trying to avoid having to do that. Or is it worthwhile doing this so that we could at least know whether -- maybe that doesn't belong in this document. But it seems to me it would be useful to the agency to have at least gone through the exercise to say, is a warning agent --

DR. BEAUVAIS: That actually -- well, when we get to the point of -- if it's determined, which this would seem to meet that case, but if it's determined that

chloropicrin requires mitigation, our general process is, when we move forward into the mitigation process, we look at individual products and mitigate products as needed. And that's where you would look at the concentration.

PANEL MEMBER HAMMOND: So it's inappropriate at this point in time.

DR. BEAUVAIS: Yeah.

PANEL MEMBER HAMMOND: Okay.

DR. BEAUVAIS: And then so what we're looking at in the risk assessment is at the active ingredient. Well, and in this case also because chloropicrin has this additional use, we're looking at the warning agent use as well.

PANEL MEMBER HAMMOND: Yeah. I mean what I'm concerned about is given --

DR. BEAUVAIS: To answer your question, would we revisit it, no, because --

PANEL MEMBER HAMMOND: We would not need to revisit it. That's what I'm trying to avoid.

DR. BEAUVAIS: If in mitigation it was determined that it could not -- you know, that active ingredient uses could not be mitigated any other way, then they would also be looking at the products with the warning agent at the same time.

PANEL MEMBER HAMMOND: I guess I want to make

sure these documents are sufficient for them to do this.

DR. BEAUVAIS: Yeah.

PANEL MEMBER HAMMOND: That's where I'm really going, is that the documents are sufficient that they don't have to start the process again, that the documents are strong enough for that.

DR. BEAUVAIS: Right.

PANEL MEMBER BYUS: And I would like to just reiterate that point very briefly. It's just unwise to use a genotoxic agent as a warning agent. I mean I -- regardless of how the numbers turn out. And you know what I mean by that. I don't mean -- but I'd say it's just an unwise mechanistic thing to do under any scenario. So I mean --

PANEL MEMBER LANDOLPH: Completely agree.

PANEL MEMBER BYUS: I mean you agree to that, right?

PANEL MEMBER LANDOLPH: Completely.

PANEL MEMBER BYUS: All right. Good.

PANEL MEMBER LANDOLPH: I have some question as to whether you want to continue to use this agent in perpetuity as a pesticide. I mean I think -- it was developed in 1908. This is 2009. I think there must be better ways to go than this type of a compound. I'm particularly concerned with the carcinogenicity and

mutagenicity of it.

And I had one more quick question.

CHAIRPERSON FROINES: Wait, wait, wait, wait.

Is Kathy -- Kathy's still on target.

PANEL MEMBER HAMMOND: And then again -- I know I keep harping on the occupation exposure piece of that. But is that going to hold up the progress of this document, since that's going to be several months down the road? And is that just what we have to do? Is that how this goes?

PANEL MEMBER GLANTZ: That's a separate process.

CHAIRPERSON FROINES: No, at the next meeting we will have our findings and we'll be done.

PANEL MEMBER HAMMOND: Okay. And they'll just do that for your own sake and for other purposes, because it's not necessary for this.

DR. BEAUVAIS: And then at that point we'll go through the typical DPR risk assessment process. It is on track going through that process, which is separate from the Toxic Air Contaminants review.

PANEL MEMBER HAMMOND: I was concerned because both the May drafts that will be available in a few months. And in the same sense as they are now. But you have plenty to do and there's a lot here.

DR. BEAUVAIS: Oh, yes.

PANEL MEMBER HAMMOND: Okay. And the new study that came in in the structural study, how did that come to your attention?

DR. BEAUVAIS: It was given to the person who's responsible for sulfuryl fluoride risk assessment, that it was actually a study to look at a new method for aeration of sulfuryl fluoride. And there was chloropicrin data in it, so then it was passed along to me. And so that's --

PANEL MEMBER HAMMOND: So it --

DR. BEAUVAIS: It was submitted by the registrant.

PANEL MEMBER HAMMOND: That's why I was just surprised that it was submitted by the registrant. But I wasn't --

DR. BEAUVAIS: And it's a well conducted study and it had data that enhanced and supplemented what we had already had from ARB.

PANEL MEMBER HAMMOND: And do you have any ideas why the values were so much higher than the ARB values?

DR. BEAUVAIS: Well, there is -- as I said, this is a proposed new aeration method. And so that would -- that would address the question about indoor air exposures.

In terms of by -- but the bystander exposures or the off-site exposures during the fumigation itself were

also higher. And I can't -- I mean I think it's simply we had three studies before and now we have another one. And, you know, it's like when you have a small number of data points, you wouldn't expect that to capture your entire population of possible --

PANEL MEMBER HAMMOND: I think that's exactly right.

DR. BEAUVAIS: So that as we get the data --

PANEL MEMBER HAMMOND: Can I do -- let me just finish --

CHAIRPERSON FROINES: Sorry.

-- just to say that I totally agree. And I think the point is that this kind of data is going to be highly scattered, there are going to be a few large points. And I think that that is an important -- it's totally credible kind of how you've given that.

CHAIRPERSON FROINES: No comments.

ARB AIR POLLUTION SPECIALIST BAKER: I can comment if you want.

CHAIRPERSON FROINES: Can't what?

ARB AIR POLLUTION SPECIALIST BAKER: If you want, I --

CHAIRPERSON FROINES: Can you come to the mike.

ARB AIR POLLUTION SPECIALIST BAKER: Lyn Baker of Air Resources Board. I can comment if you want.

I would speculate that our monitoring results around the structural fumigation studies were lower than the industry studies because we only deployed a few samplers. And at the time of the studies, we had to expect where the wind was going to take the sulfuryl fluoride and the chloropicrin. And we probably didn't put the samplers exactly where the peak concentrations went.

Where the industry studies, as Terri and Sheryl showed, had three or four samplers in several directions around the homes, had a lot higher probability of catching the highest concentrations. And even those studies may not have captured the peak concentrations. Situations where you've been modeling actually may be more worst case than monitoring data.

PANEL MEMBER HAMMOND: Oh, I think they're both important.

May I request possibly a little paragraph to that extent that explains some of that could be included as well.

And then the other thing just -- it just strikes me, is if you have a little tent up there around a house, I understand on the one hand thinking that five feet might be, you know, too close for bystanders. But I think kids in the neighborhood might find it really fascinating, you know, and might really be near there. So I don't think

it's an unreasonable value.

CHAIRPERSON FROINES: Thanks, Lyn.

Kathy.

PANEL MEMBER HAMMOND: So I think there's an excellent job here. And that's really it for now.

CHAIRPERSON FROINES: Great.

Paul.

PANEL MEMBER BLANC: Well, as a procedural or practical matter, one thing I would suggest is that if you could quickly make a list in follow-up to this meeting of the points that you're -- the changes that you anticipate for both the exposure assessment and health assessment based on what we've discussed today, and if we could get those not only back to the panel but actually back to OEHHA. What I'd like to do is see some of the OEHHA -- I'd like to see OEHHA revisit their document in light of those, because it seemed to me that you addressed most of their major points.

In terms of the OEHHA document, aside from that, one of the -- the OEHHA critique was not as useful to me as it might have been because it had a mixture of things which seemed to be summaries of what DPA was saying, then there were sections which seemed to be a critique but then didn't actually say whether something needed to be changed, and then there were parts which either ended with

saying, "Therefore, we agree with what OEHHA did" or "Therefore, we would recommend such and such."

So I think different people wrote different sections of the OEHHA evaluation. That's my guess. And I think it needed firmer overall editorial hands to make it more useful.

So I don't want you to rewrite it now. What I want you to do is take the responses of the DPA, then go back to your document and say what you think is still unresolved or not. And is that okay, the way to go forward?

Also would say that it's probably not worth going into a lengthy critique and then having a last sentence that says but in the end you would come to the same value anyway. I mean that's really not -- probably not that productive a use of energy.

I think that the document overall is -- errs on the side of being health protective where choices are needed, does a thorough job of health effects review, is logical and stepwise.

And I think that your responses in your written comments in terms of response to the industry critique, which was then reforwarded to the review panel also independently of your comments to it, were I thought convincing and I believe that the major issues were

addressed. I think you have to consider ways in which the text of the document, to the extent that it can, can have slight modifications which build into it those responses.

Obviously in your document you don't want to say, "and in response to such and such..." But if there's a clarification, for example, in regards to the use of the life-expectancy-adjusted trend test and the issue of can this be applied to this species, I think you should simply say in your methods, "We applied it to this species, whether we don't believe there's any reason that" -- you know, whatever in your sort of methodologic issues. So try to build in those things and take into account if you have other comments that you -- in the committee today about the carcinogenicity being biologically plausible and the mutagenicity and so forth. And I think --

CHAIRPERSON FROINES: Paul, can I comment on that?

PANEL MEMBER BLANC: Yeah.

CHAIRPERSON FROINES: The document at the end says something to the effect that the chloropicrin may possibly be genotoxic. I think the word "possibly" is one of those words that really doesn't have a lot of meaning to it.

I would -- because we are making fairly major conclusions about carcinogenicity and genotoxicity in the

document overall, I would say something to the effect that chloropicrin appears to be likely a genotoxic compound, rather than possibly. It's too wishy-washy for the level of data.

PANEL MEMBER BLANC: Well, or you can use the terminology "more likely than not," if you think the weight of the evidence is more in favor than more against. You know, people could argue what does "likely" mean also. Is it a 80 percent likelihood or 90 percent --

CHAIRPERSON FROINES: "More likely than not," that sounds like a good compromise.

PANEL MEMBER BLANC: But I think you've heard some rationale here as to why that's the case.

I do think that your executive summary needs to be retooled, because there were changes that occurred but they're not reflected in the executive summary. You know, one example being the comments that you made that you have new data now on the photo reactivity indicating that the bulk of the photo reactivity went to nitrogen dioxide. And that wasn't really reflected in the executive summary. For example, the executive summary still talked about photo reactions with phosgene and other things. That's also true of OEHHA's comments, having -- you know, caught up with that.

So, overall, I think that it's -- you know,

there's absolutely no question that this is a toxic air contaminant -- meets the criteria for a toxic air contaminant. I think that you have to view some of these exercises that you're going through as laying the groundwork for when you do other assessments which may be closer to the cusp of saying something's a toxic air contaminant. So I don't want you to feel that this is just busy work because -- just say, "Well, you know, by a factor of 10,000 this is going to be a toxic air contaminant. So why do you care if I do benchmark 2.5 versus 5.0? You know, does it really matter?"

And so I think it just for those reasons, if nothing else, will help you. But I do think that it marks a sea change in the approach of the agency to the good -- to the public health good.

And I think it also demonstrates a much closer drawing together of the OEHHA approach and the DPR approach. I think the fact that their summary comments were so wordy actually understates how close the two agencies or two groups are, because before their findings would be, "that's no good, that's no good that's no good," as much -- they could be much briefer because of this.

(Laughter.)

PANEL MEMBER GLANTZ: Can I just inject.

I agree with what Paul's saying. But, you know,

getting back to the point Kathy made about the warning -- using this as a warning chemical.

I mean as I read this, there's maybe a factor of maybe 20 to 100 difference between the use of chloropicrin as a warning compound versus the active ingredient. And we're talking about a factor of 10,000.

So I think it should -- I think it wouldn't be that hard based on the presentations today and the feedback that you've got to just add in -- since you're -- you know, you've listed these other three things. I would add a forth one, which is the warning, saying --

CHAIRPERSON FROINES: Stan, Paul has five minutes.

PANEL MEMBER BYUS: We all have five minutes.

And I think that's reasonable. I think that basically what you can say is that even if on the exposure side it was 120th the amount, if you reduced that by 120th, your MOE would still be a hundredfold above the threshold for saying it's -- I think that's what Stan was just trying the say. So --

CHAIRPERSON FROINES: Can I ask a question that's a little premature?

There are one, two, three, four, five -- six people who haven't discussed the document.

I'm assuming that you would like to vote -- this

is a toxic air -- because the changes are relatively minor that are being requested. And I'm assuming -- but I want to ask the question: Do you want to vote on this as a TAC now or do you want to have an opportunity to discuss it at the next meeting before a vote?

PANEL MEMBER GLANTZ: I'm comfortable voting now.

PANEL MEMBER FRIEDMAN: Me too. I have no further questions or comments.

PANEL MEMBER GLANTZ: But I don't have any other questions or comments?

PANEL MEMBER LANDOLPH: Same.

CHAIRPERSON FROINES: So can somebody make a motion?

PANEL MEMBER LANDOLPH: I make a motion that we vote to recommend that TAC -- that chloropicrin be listed as a toxic air contaminant.

PANEL MEMBER HAMMOND: Second it.

CHAIRPERSON FROINES: All in favor?

(Hands raised.)

CHAIRPERSON FROINES: We're unanimous.

We actually have done a compound in one meeting. This is a first.

PANEL MEMBER HAMMOND: Thanks to your excellent work.

PANEL MEMBER BYUS: Thanks to your excellent

work.

PANEL MEMBER FRIEDMAN: This group did a great job presenting this -- the beautiful presentations that you both made. So thanks very much.

CHAIRPERSON FROINES: So, folks, we're done for the day if somebody will make a motion to adjourn.

PANEL MEMBER BYUS: I might add that Joe here has done an outstanding job on written comments.

Which you've given to them too, right?

PANEL MEMBER LANDOLPH: Yeah. And I re-revised them today.

CHAIRPERSON FROINES: If anybody has other comments, they should get them to me, and I will get them to DPR, so we can come in to the next meeting with any other -- any other questions can be dealt with by DPR during the time between now and then.

PANEL MEMBER HAMMOND: And we're supposed to work on findings; is that correct?

CHAIRPERSON FROINES: Yes.

PANEL MEMBER HAMMOND: Paul and I.

CHAIRPERSON FROINES: And we're going to try and keep --

PANEL MEMBER BLANC: Well, the findings will be very brief.

CHAIRPERSON FROINES: Well, we want them to be

brief.

PANEL MEMBER HAMMOND: But you do want to have some very specific things.

PANEL MEMBER BLANC: I think they'll be very, very brief.

CHAIRPERSON FROINES: If I know Paul Blanc, I'm not worried about the length of this document.

PANEL MEMBER GLANTZ: Can I get a ride with you?

CHAIRPERSON FROINES: Did we adjourn?

Wait, wait, wait.

PANEL MEMBER BLANC: Yes, I move we adjourn.

PANEL MEMBER HAMMOND: Second.

PANEL MEMBER BLANC: All in favor?

(Ayes.)

CHAIRPERSON FROINES: We're adjourned.

(Thereupon the California Air Resources Board, Scientific Review Panel adjourned at 2:00 p.m.)

CERTIFICATE OF REPORTER

I, JAMES F. PETERS, a Certified Shorthand Reporter of the State of California, and Registered Professional Reporter, do hereby certify:

That I am a disinterested person herein; that the foregoing California Air Resources Board, Scientific Review Panel meeting was reported in shorthand by me, James F. Peters, a Certified Shorthand Reporter of the State of California;

That the said proceedings was taken before me, in shorthand writing, and was thereafter transcribed, under my direction, by computer-assisted transcription.

I further certify that I am not of counsel or attorney for any of the parties to said hearing nor in any way interested in the outcome of said hearing.

IN WITNESS WHEREOF, I have hereunto set my hand this 23rd day of December, 2009.

JAMES F. PETERS, CSR, RPR
Certified Shorthand Reporter
License No. 10063