SCIENTIFIC REVIEW PANEL ON TOXIC AIR CONTAMINANTS

STATE OF CALIFORNIA

PUBLIC MEETING

TRANSCRIPT OF PROCEEDINGS

April 27, 2001

10:14 A.M.

Tom Bradley International Hall
University of California, Los Angeles
417 Charles Young Drive West
Los Angeles, California

REPORTED BY:
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APPEARANCES:

SCIENTIFIC REVIEW PANEL

Dr. John Froines, Chairman
Dr. Roger Atkinson
Dr. Paul Blanc
Dr. Craig Byus
Dr. Stanton Glantz
Dr. Gary Friedman
Dr. Anthony Fucaloro

REPRESENTING THE CALIFORNIA AIR RESOURCES CONTROL BOARD:

Mr. Jim Behrmann, Liaison, Scientific Review Panel
Mr. Peter Mathews, Assistant to the Liaison
Mr. Kirk Oliver, Attorney

REPRESENTING THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT:

Dr. George Alexeeff, Deputy Director for Scientific Affairs
Dr. Melanie Marty, Senior Toxicologist
Dr. James Collins, Staff Toxicologist
Dr. Andrew Salmon, Chief, Air Toxicology and Risk Assessment Unit
Dr. Thomas McDonald, Staff Toxicologist
Dr. Stanley Dawson, Staff Toxicologist
Ms. Judy Polakoff, Associate Toxicologist
Dr. Bruce Winder, Associate Toxicologist

ALSO PRESENT:

Dr. Mark Miller
Dr. David Morry

A G E N D A

CHAIRMAN FROINES: I would like to call to order the Scientific Review Panel meeting for April 27th, 2001 officially.

The first item to -- for discussion is not on the agenda, and it's meant as a very informal comment by Dr. Byus on the progress with respect to the organophosphate document.

DR. BYUS: Thanks, John.

CHAIRMAN FROINES: And no action will follow from this update.

DR. BYUS: They were proceeding -- I've received two of the chapters so far and have had conference calls on both of them. That's proceeding quite well. They've updated their schedule to me, which I gave to the panel, Jim and to John.

And so we're proceeding quite quickly on those documents. It looks like we're going to meet the schedule that they had originally given us. So that's all they wanted me to tell you at the meeting since they couldn't be here.

CHAIRMAN FROINES: The second item -- I've passed out -- I think everybody -- if there's anybody who's missing a copy, please let me know -- of the draft agenda for the scientific meeting on issues in the assessment of health impacts of gasoline emissions in

California, which is scheduled for June 12th and 13th this year. And I think it's an absolutely outstanding agenda, so we would urge interested scientists and professionals to attend the meeting. It's sponsored by OEHHA, and it will be held at UCLA.

After those bookkeeping, I am going to turn the meeting at this point over to Melanie, Dr. Melanie Marty, to discuss the children's environmental health compounds.

DR. MARTY: Good morning. Is this mike on?

DR. GLANTZ: Yeah.

CHAIRMAN FROINES: I think -- let me just give the ground rules. I think what we're going to do -- Melanie, tell me if you don't agree -- we're going to -- Melanie is going to present the criteria and give an overview of the process to begin with, and then we can have questions during that time and subsequent to it, and then we'll proceed to address the individual chemicals on a one-by-one basis.

We haven't assigned lead status to anyone on the panel for a particular chemical, so as we are discussing a particular chemical, we'll go around the room and have input from the panel in order.

So is that your sense of it --

DR. MARTY: Yes.

CHAIRMAN FROINES: -- Melanie? Go ahead.

DR. MARTY: Okay. Today we're going to talk about a document we drafted, the prioritization of toxic air contaminants, under Senate Bill 25, which is the Children's Environmental Health Protection Act.

I just thought I'd start -- next slide, please. The miracles of modern technology.

(Pause.)

DR. MARTY: Okay. I thought I'd start with just some quotes from the statute about what we're supposed to be doing. The office, which is OEHHA, in consultation with the state board, which is the Air Resources Board, shall establish a list of up to five toxic air contaminants -- and these were specifically that had already been identified under existing statutes -- that may cause infants and children to be especially susceptible to illness.

In developing the list, the law requires us to take into account public exposures to toxic air contaminants, whether by themselves or interacting with other toxic air contaminants or criteria air pollutants.

And then there were four specific factors that the law requires us to evaluate. Next slide, please. These factors include exposure patterns among infants and children that are likely to result in

disproportionately high exposures; special susceptibility of infants and children to air pollutants in comparison to overall general population; the effects infants and children of exposures to TACs and other substances with a common mechanism of action; and, finally, the interaction of multiple pollutants, including the interactions between criteria pollutants and toxic air contaminants.

CHAIRMAN FROINES: Just one point. Andy, could you go back to the previous slide?

I think it's important to bring to the panel's attention that the -- that the words on the -- under the first bullet are "that may cause infants and children to be especially susceptible to illness." So the word "may" of course is a problem in some respects because it is -- it doesn't define the scientific rigor associated with that decision. So the panel needs to be aware of that designation.

Sorry.

DR. MARTY: What happens after OEHHA establishes this list is that the ARB steps in. They must within two years evaluate existing control measures. Those are the airborne toxic control measures, or ATCMS, for substances on the list and revise them, if appropriate.

If there is not an ATCM for a substance that gets on the list, then ARB within three years must prepare what they call a "needs assessment" or a report on the need for regulations for those TACs and adopt them if it's appropriate.

DR. GLANTZ: Melanie, I just have a question. Of the 11 compounds that you suggested in the Tier 1 and Tier 2, are there any of them that ARB doesn't have toxic control measures for?

DR. MARTY: Yes.

DR. GLANTZ: Which ones?

DR. MARTY: I was afraid you were going to ask me that.

DR. GLANTZ: I mean, it's not -- it's a little bit off the subject, but I'd be just curious.

DR. MARTY: Okay. And ARB can correct me if I'm wrong. Formaldehyde, lead, polycyclic aromatic hydrocarbons, acrolein, glycol, ethers. They're working on diesel. Mercury there is not one, PCBs or vinyl chloride. So --

CHAIRMAN FROINES: Dioxins?

DR. MARTY: -- most of them. Dioxins, there is a control measure from -- for emissions from medical waste incinerators.

DR. GLANTZ: Okay.

CHAIRMAN FROINES: Can somebody write down that list and give it to the panel?

DR. GLANTZ: Well, it's in the transcript.

CHAIRMAN FROINES: No. I mean the ones that don't have control measures.

It's all right. Go ahead.

DR. MARTY: Next slide, Andy.

What I'd like to do now is talk about our prioritization activity, how did we start with over 200 TACs, depending on how you count them, and work down to the list of 11 and then the list of 5 proposed. We started with a list of all 200 TACs, and we actually have that list if the panel wants it to go through it.

Peter, do you want to hand out those lists?

We started with a list of TACs. And, actually, it was a summary table from ARB's prioritization process that they used to come up with candidates for us to look at health effects. So we started out with the TACs and information on ambient concentration data.

We updated that data, if there were new data available from the ARB's monitoring network, for example. We divided the ambient concentration data by a chronic reference exposure level and then ranked the chemicals in order of that ratio.

What this does is gives you an indication of

where the ambient concentrations that have been measured are with respect to a benchmark that you consider a safe dose. So that's what we tried to do to see, okay, are any of these actually above our chronic reference exposure level, or are any of them close to our chronic reference exposure level?

We also wanted to deal with the carcinogenicity piece, so we multiplied the ambient concentration data by available unit risk factors to rank the carcinogens by ambient cancer risk.

The chemicals -- since we're not charged with having a list of carcinogens and a separate list for non-carcinogens, we have to combine those two rankings. So the chemicals were placed on single lists, and depending on the ratio of the ambient data to the REL or the product of the URF times the ambient concentration, they were moved up or down in the ranking according to which really drove the risk for that chemical.

DR. FRIEDMAN: Could you give a numerical example of that to make it a little bit clearer?

DR. MARTY: You know what?

CHAIRMAN FROINES: I can.

DR. MARTY: Table --

CHAIRMAN FROINES: I can.

DR. MARTY: Okay.

CHAIRMAN FROINES: Acrolein has a -- in their document has a 14.3 microgram per cubic meter is the most recent exposure level. It is when you take that value and divide the air concentration by the REL, you get a ratio of 238. Whereas the ratio for formaldehyde is 1.1. The ratio of arsenic is .5 and then toluene, for example, is .025, so that -- methyl chloroform, for example, goes to .0005, so there's a very wide range of air concentrations relative to the REL value, and there's a lot of air concentrations that are missing.

DR. FRIEDMAN: Well, the question I had was not that but how you merged the cancer potency and that ratio. How you -- you know, how you then ranked -- came up with the ranking on a single list.

DR. MARTY: Okay. The -- there were only really a few cases where it was obvious. If that ratio of the ambient concentration to the REL was extremely small, who cares?

DR. FRIEDMAN: Right.

DR. MARTY: So the cancer risk would drive it in that case.

DR. FRIEDMAN: So you -- in other words, if the cancer risk was bigger than that other ratio, you selected that as the number with which to rank all the chemicals?

DR. MARTY: Yes. In a sense. They're different -- they're measures of different things, so there is some judgment that you have to use: Is that cancer risk more of a concern than the reference exposure level? And generally the answer to that is yes because the thresholds are assumed -- that are assumed for non-cancer endpoints means that if you're below that REL, you're pretty -- pretty confident that it's an okay exposure to be -- an okay concentration to be exposed to.

Whereas the cancers are assumed to be linear related, so what you have there is you have a probability of cancer risk. And it may mean that neither of them is really very important, but if one was more important than the other, it would push up in the ranking.

DR. FRIEDMAN: And when you say "more important," do you mean a higher -- just a higher ratio?

DR. MARTY: A high -- a ratio that would, for example, approach .5 or even .1 for the ratio of the concentration to the REL. That to me would be more important than something that had a cancer risk of 10 to the minus 8. So it's -- it's because --

DR. FRIEDMAN: Was there ever a case when the cancer risk moved the chemical up higher on the ranking?

DR. MARTY: I'm sure that's true.

DR. MORRY: There are one or two cases like that. So we had two lists. One ranked by cancer risk, one ranked by non-cancer endpoints. A lot of chemicals were the same on both lists, and, in general, the order was the same where the chemicals appeared on both list. It was just a matter of putting them in register with each other.

And in a few cases you've got to decide, well, you've got some non-cancer values and some cancer values that are sort of in the same part of the list, and which one do you put above -- which chemical do you put above another chemical? So there's a little bit of arbitrariness in doing that. But it's just -- the arbitrariness would only affect up or down.

DR. MARTY: Judgment day. A little bit of the judgment.

DR. MORRY: Okay. But the judgment would only taint it up or down, like, a few positions.

DR. FRIEDMAN: I see. I think, you know, in some of the comments, the public comments, about the lack of transparency, I think this is one area where it isn't totally transparent especially when you say that, you know, there's a matter of judgment there, and the criteria aren't quite clear.

DR. MARTY: I think what we want to do is -- go ahead, Stan.

DR. GLANTZ: Well, I had a long discussion with Melanie and her people about this. I agree that several of the public commenters commented on the lack of transparency, and I think that's a problem. I think that the process isn't quite as irrational as it looked, the way they described it, when I sat down and had them explain it.

And what I would propose doing is let Melanie finish talking, this part of the talk where you're just talking about the prioritization, and then I think we should just stop and discuss that and then go on to the other chemicals.

CHAIRMAN FROINES: I think it's important -- I think it's important to have a specific discussion --

DR. GLANTZ: Yeah.

CHAIRMAN FROINES: -- about the document and --

DR. GLANTZ: Yeah. I mean, I --

CHAIRMAN FROINES: -- and the methodology.

DR. GLANTZ: Yeah. I mean after discussing it with them, I think the prioritization procedure that they used was pretty reasonable, but the way it was described, it was completely opaque. And so what I'd like to do is just let her finish this part of it, and

then I think we should discuss this and bring out exactly how it was done.

And I had given Melanie a couple of suggestions of ways I think it ought to be presented, which would, I think, make people a lot more comfortable.

DR. MARTY: I actually prepared some tables at the request of Stan, which will probably shed some light onto this and which we can put into the document when we revise it and make it clearer of what it is that we actually did.

DR. GLANTZ: Why don't you just finish this part of the presentation.

CHAIRMAN FROINES: I have one question, if Peter is in the room or Jim. Do we have access to a Xerox machine because I do have the document that lists all these values?

DR. MARTY: We have that as a handout.

CHAIRMAN FROINES: You do. Okay.

DR. MARTY: So we need to get -- and you --

DR. BYUS: You must have sent it to us.

DR. MARTY: Yes. We sent that to the panel with the document.

DR. GLANTZ: Yeah. But I actually don't find that as helpful as -- why don't -- just let her finish.

CHAIRMAN FROINES: Let's go ahead. But just so

for everybody on the panel, you have the document.

DR. GLANTZ: Well, that is a document, but I personally didn't find that -- that's not what I think should be presented. But, anyway, why don't, Melanie -- why don't you just finish this part of the presentation, and then we can begin pondering.

DR. MARTY: Okay. There were some chemicals that had unit risk factors but no reference exposure levels, so we dealt with those by, again, multiplying the unit risk factor by the ambient concentration data, and then we positioned those tables according to the product of that with respect to the other carcinogens in the table.

Next slide, please. This initial procedure provides a ranking based on existing health criteria, existing reference exposure levels and existing unit risk factors and the ambient concentration data. Since there are some chemicals for which there are no ambient concentration data readily available, we wanted to look at other indications that there is exposure in California.

So we evaluated other sources of exposure information, which included the Air Toxics Hot Spots emissions inventory database. There's over 30,000 facilities in that database, and the emissions are not

something that you can readily translate into a concentration, but you can get an idea in terms of pounds per year of how much of these chemicals are being emitted by facilities in California.

We also looked at the mobile source emissions database to get an idea of which chemicals from a mobile source perspective are important.

After doing that, we still needed to consider toxicological properties and whether or not there is a known sensitivity of young organisms relative to old organisms, old people, adults, for that particular toxic chemical. So we also took that into consideration.

Andy, I think I'm on the next slide.

DR. MARTY: So we took into consideration --

DR. SALMON: Sorry.

DR. MARTY: Go back one. We took into consideration the emissions inventories from mobile and stationary sources. We reviewed the entire list of TACs, not just those that had ambient concentration data, to look for any chemicals with known toxicological properties that would be of concern. For example, mercury, we didn't have good ambient concentration for mercury.

And over half of the TACs dropped out at this point.

DR. BLANC: Because?

DR. MARTY: Because they either had -- Table A, which is being passed out to you, is a list of all the TACs.

DR. BLANC: Right.

DR. MARTY: Table B is a list of the chemicals that dropped out at this stage of the game.

DR. BLANC: Because you did not have ambient data.

DR. MARTY: We didn't have either ambient data or any information on emissions, and/or we did not have unit risk factor or chronic level exposure levels. So for some of those, all of those apply.

DR. BLANC: Doesn't the actual legislation refer to exposures or potential exposures in its language?

DR. MARTY: Well, I have the statute in front of me.

DR. BLANC: Potential and --

DR. MARTY: The potential exposures would be taken care of by looking at emissions inventory data. Is this stuff even emitted in California? Is it an airborne chemical in California?

DR. BLANC: Well, let me ask you if you thought something was about to enter into the marketplace on a

mass scale, wouldn't that represent a potential exposure, or if something for which you don't have quantified release data and yet you would know from some other source that it must be released? Wouldn't that be --

DR. MARTY: Well, we did talk to the Air Resources Board to get at precisely those issues, but there were no hard data to go on to take care of those contingencies.

DR. BLANC: Well, wouldn't that, in fact, be an area where there wouldn't be hard data, or what does hard data mean to you in that situation?

DR. MARTY: Either an indication of -- they're an emission inventory, pounds per year from a certain facility, or something that's been looked at from the mobile source side of things in terms of the mobile source emissions inventory. Neither of those inventories is perfect.

For example, the hot spots facility emission inventory, they inventory about 425 chemicals. Some of those emissions estimates are just that. They're estimates. They're based on throughput of the facility. They're based on use by the facility, and those are not perfect estimates of emissions by stretch.

And there may be chemicals which are not being

reported. Although, in this case, for the TACs, they're all substances which need to be reported under the Air Toxic Hot Spots.

In the case of the mobile source emissions inventory, yes, we know about benzene and butadiene and formaldehyde and the more common chemicals that we're concerned about from mobile sources, but there may be some that no one's looking at.

DR. BLANC: Well, if you don't mind, let me just ask the specific case examples that I can -- as a way of clarifying your thinking. There is a lot of concern about the potential introduction of organified manganese as a gasoline additive, as you're aware. Manganese is a neurotoxin for which there would be a lot of rationale for considering --

DR. MARTY: Yes.

DR. BLANC: -- pediatric sensitivity. Manganese is a -- manganese and manganese compounds are TACs. By what criterion would one eliminate or not eliminate manganese from being on the list of things to be given a great deal of consideration?

DR. MARTY: We actually put manganese into the top 35 that we did literature reviews for, for precisely that reason.

DR. BLANC: And then what happened?

DR. GLANTZ: Well --

DR. MARTY: Let me get there.

DR. BLANC: So -- but by your criteria, that wouldn't be --

DR. GLANTZ: Having spent a lot of time giving Melanie and her staff a very hard time about this, I really think we would have a more productive discussion if you let her just finish describing what they did.

DR. BLANC: Well, that was the nature of my question. I wanted to understand the process by focusing on the sample, and I'm going to actually keep -- I'm going to continue, over the course of the morning, be returning to specific examples so that I can understand how those fit into your process.

DR. MARTY: Sure.

Okay. Does the panel have the tables yet?

CHAIRMAN FROINES: Yeah, we do.

DR. MARTY: Table A is just a list of the TACs, so you can put that on the bottom of your pile now. Table B is a list of the chemicals that fell out because there were no indications of exposure either from emissions inventories or ambient concentration data, or there were no health criteria, no RELs, no unit risk factors.

DR. GLANTZ: I have one -- I'm not breaking my

own rule, but I just have a question on a case.

CHAIRMAN FROINES: Yes, you are.

DR. GLANTZ: No, I'm not.

DR. BYUS: You are.

DR. GLANTZ: Only Dr. Freud is allowed to do that. Anyway, when you say for which there are no RELs, cancer potency factors and adequate ambient air levels data, does that mean that if you didn't meet -- what if you had something that was like -- had huge cancer potency but there was no REL? That wouldn't drop out?

DR. MARTY: No. That didn't. That wouldn't drop out.

DR. GLANTZ: So that's really -- so I think -- so you're -- given the sensitivities about how this list was made, I mean, I think we need to be very precise here. So of the stuff in Table B, of however many are in here, 137 compounds here, how many of these are on this list because you couldn't find any evidence of exposure in California?

DR. MARTY: I would say the vast majority.

DR. ATKINSON: Many of those are probably either constituents of gasoline or some are formed in the atmosphere where there's really going to be exposure. But there may be no actual emissions data; is that right?

DR. MARTY: That's a problem, yes. Yeah. And many of these do not have health values, so there's no handle on the toxicity in a quantitative sense.

DR. GLANTZ: Well, I think one thing, again, and getting to the point of making this as transparent as possible, I would suggest that you break Table B up into pieces, and I would have -- the ones for which you have no evidence of emission, that is one list. So you can say to people, we excluded these -- not withstanding what Roger just said, because we couldn't find any evidence that it's being released into the air and then that's very clear; okay? That that's why you're not looking at those.

And then I think if -- for the ones where you have no data documenting health impacts, I would have that as a separate sublist.

DR. MARTY: Okay. I wouldn't say that there were no data --

DR. GLANTZ: Well --

DR. MARTY: -- documenting health impacts, but rather there was no quantitative assessment of those chemicals.

DR. GLANTZ: Okay.

DR. MARTY: There are chemicals that initially were on Table B that we moved up because of concerns

about --

DR. GLANTZ: Okay. But that's moving it -- I mean, the question -- the concern I think is what are you dropping off the list and why? And then we'll get -- when you get down to the short list, that's, of course, where the biggest debates come. But I think to just say we didn't include these because there was no evidence of emission, and then the rest of these, within this list, which ones you didn't include because you didn't have a unit risk or a REL. And that way it's very clear why these are not here.

Now, that doesn't mean that, if you look at the point that Paul made, that if something's about to be emitted, you could put it on a higher list. But, you know, that at least explains where this list came from.

I really think -- I mean, when I read through all the comments, this issue of making the process really transparent is absolutely crucial for people, you know, buying into this document. And the -- and it's -- I realize when you go from 200 to 5 or 11 and given that there's apples and oranges aspects of this, you do have to apply some judgment. But I just think the more explicit you can make all of that, the more comfortable people will be with the outcome. So that would be my suggestion for this.

DR. MARTY: Okay.

DR. GLANTZ: So now I'll let you go ahead with the presentation.

CHAIRMAN FROINES: I think, as a generality, a point that needs to be made is that any member of the public should be able to look at the 200 TACs and understand why it's where it is on the list because I think -- I think these lists are not adequate at this point and -- but at some point in the future we just need to make sure that anybody in the audience can pick it up and say, "Oh, I may not agree with why this is where it is, but I understand why" --

DR. MARTY: Why it's where it is.

CHAIRMAN FROINES: -- "it's where it is."

DR. BLANC: So, just to clarify again for the specific chemicals, I understand as it relates to your comment that I can't tell from this list why something fell out, but parathion, for example, is that because it's no longer in use? It's a banned pesticide.

DR. MARTY: Actually, there were two issues there. One is with pesticides in general. This statute only applied to the TACs that were not pesticides. In other words, they did not --

Jim, can you help me out here?

DR. BLANC: It doesn't say that in the

legislation explicitly. It says something obliquely. Have you had legal counsel actually make that extremely clear?

DR. MARTY: ARB's legal counsel made that --

DR. BLANC: In writing and that's included in your document?

DR. MARTY: It's not in writing, and it's not included in the document.

DR. BLANC: Well, I would say that any member of the public who opens up the document and suddenly sees that there are not pesticides and no -- particularly no acetylcholinesterase inhibitors included.

In fact, I would say that based on a narrow reading of the statute -- first of all, I don't necessarily agree with that interpretation based on what I've read, but I would say even if that was correct in the narrow sense, isn't it also true that it refers only to -- the line that must have been interpreted in that way refers to pesticides in their pesticidal uses.

So if there was any cholinesterase inhibitor, let's say, that was ever used for any reason that was not pesticidal and if it would be combined with the effects of exposures that wouldn't fall under your statute, you're supposed to consider that too as a

cumulative issue.

DR. MARTY: I can't really answer that. You know, all I can say is what the attorneys have told me is that this statute does not apply to the TACs that are identified by DPR's director.

DR. BLANC: And yet your text says, "We looked at all TACs." It doesn't say we looked at all TACs except those TACs which involve pesticides.

DR. MARTY: It's because we actually did, but as the process evolved realized we couldn't handle the pesticides under this statute.

CHAIRMAN FROINES: I think that the problem with, also, I think what Paul's raising in part, is that if you have a chemical manufacturing company that makes pesticides, then they would fall under this statute and should not be excluded.

DR. MARTY: The other issue is that there are not very much data on ambient concentrations of pesticides. So within the paradigm we used, it's not particularly easy to deal with the exposure aspect for the pesticides, but there are -- you know, I can't argue the law because I'm not a lawyer, but this is just what we've been told. We can't.

DR. ALEXEEFF: George Alexeeff here with OEHHA. If you look on page A-12, this is where we're actually

quoting. We have a copy of the statute in here.

CHAIRMAN FROINES: Yes.

DR. ALEXEEFF: And go down to subsection D; okay? And now we're in the part about the listing, just the listing part, what we're talking about today and putting things on this children's related list. It says, "Toxic air contaminants evaluated and listed pursuant to this section shall not include substances in those uses that are not subject to regulation by the state board pursuant to this chapter."

So it does refer to, in part, what you were just saying about the pesticidal use, but, basically, we're restricted to those uses which the Air Board can regulate. Now, we can make that clearer in the document.

CHAIRMAN FROINES: But, Paul -- I mean, pardon me, George, we identified ethylene dibromide as a TAC, not through the Air Board but through the -- not through the DPR but through the Air Board.

DR. ALEXEEFF: Correct.

CHAIRMAN FROINES: So that, in fact, there are chemicals that are used or produced or formulated which are pesticides but are -- which would then fall under that designation of the state board.

DR. ALEXEEFF: Correct. Correct. And we tried

to retain those. So we could try to clarify that as well in the list, which ones fell out, because of -- to our knowledge, they were only emitted in their pesticidal use.

DR. MARTY: Okay. I did want to --

CHAIRMAN FROINES: I think it's important to stress for everybody in the audience and on the panel that this is the first time any state or agency or federal government has attempted to identify compounds on the basis of their differential susceptibility, so we are -- this is going to be under a real microscope, so we really want to be sure to do it as well as we can. So I think this is -- everybody should be prepared. This is going to be a long day.

DR. MARTY: Okay. I did want to --

DR. GLANTZ: Especially for Melanie.

DR. MARTY: I did want to point out some of the chemicals that we put back on the list, even though they didn't make these initial cuts asbestos, a carcinogen with a very long latency; carbon disulfide, we're concerned about neuro and repro developmental toxs; glycol ethers, which are known developmental toxicants; and hexane, we didn't have good data in terms of ambient concentrations, but there are several large sources of hexane in the state that are stationary sources, and

it's a peripheral nervous system intoxicant.

Isocyanates, there are -- we don't have good ambient concentration data. There are a number of sources -- stationary sources of isocyanates in this state. They're potent sensitizers, so we're concerned about those from an immuno-toxic perspective.

Mercury, we didn't have good data, but mercury is a well-known developmental neurotoxicant. There is widespread exposure in California. Although, it's largely -- it's not necessarily from mercury that was initially airborne.

And then we actually also added back in ethyl ketone because of widespread emissions and potential for increased use in consumer products because U.S. EPA may list -- delist it as an ozone reactive volatile organic.

DR. ATKINSON: So you mentioned hexane coming back in. Hexane is just one of many gasoline ingredients, so anything else that's got as much toxicity as hexane would probably be -- you'd get about as much exposure, depending on how much is in the gasoline. Even if there's no --

DR. MARTY: Yeah. Most of the important chemicals in gasoline -- important in terms of we know what -- something about their toxicity, did actually end up in the final 35 that we did literature reviews on.

CHAIRMAN FROINES: We don't have that list.

DR. MARTY: You don't. I'm sorry. I meant to put it as a slide and I didn't.

DR. GLANTZ: Yeah, we do. The 35? That's Table D.

DR. MARTY: Oh. But I think what John means is we don't have the list that I just rattled off.

DR. GLANTZ: Yeah. Well, I was going to suggest that when you get the transcript, you can copy it into the document. That would be very helpful.

DR. MARTY: Okay.

DR. GLANTZ: I mean, this gets back to really making it -- I mean, I think the reasons that you stated, Melanie, were very reasonable, and I think you need to state those in the document for people to see that's why you did it. It wasn't arbitrary. Those are -- I think what you said is very sensible. It just needs to be said in the document.

DR. MARTY: Okay. Table C, which is in front of you, shows the 95 that did make it past this first cut.

DR. BLANC: Table which? I'm sorry.

DR. MARTY: C. And it's alphabetical order. It's not an indication of the ranking. You also have Table 1, which is the ranking, which I think all of you

have already seen because we sent it to the panel with the document.

But I do want to point out that the quantitative ranking we did based on ambient concentration data, reference exposure levels and unit risk factors has limited utility in terms of prioritizing for TACs that may impact children. The health criterion aren't necessarily developed around an endpoint that may impact children.

So it's -- you're dealing with existing information. There's lots of newer information in the literature that we needed to look at, which is why we did the focus literature reviews.

Andy, could I have the next slide?

DR. GLANTZ: Now, the order in Table 1 that you gave us now, these are ordered by the chronic -- the air concentration over the REL and the risk. You took that and then you took -- so you took the air concentration over the REL and the unit risk times the air concentration, and those are the last two columns.

DR. MARTY: Yes.

DR. GLANTZ: And then I'm just trying to make sure I understand this. And then you sorted the list based on the air concentration over the REL, and then you went down and looked at the risk times the air

concentration, and if you had something that the first sort seemed to put in the wrong place, you then moved -- you applied judgment to move it up or down.

DR. MARTY: Right.

DR. GLANTZ: To sort of balance the two different outcomes.

DR. MARTY: Right. And --

DR. GLANTZ: So that's how you ended up with this -- with this list, and these are not alphabetical order. These are in the order of this --

DR. MARTY: They're pretty much in the order by the air concentration over REL. They're not necessarily in order by cancer risk.

DR. BLANC: Which list now? I'm sorry.

DR. MARTY: This is Table 1. It's the list that has the --

DR. BLANC: Okay.

DR. GLANTZ: And that's the 95 then; right?

DR. MARTY: Yes. There's actually some that didn't -- that ended up in the 95 that are not scored here due to lack of ambient concentration data.

DR. GLANTZ: And then can you tell us -- when you did the air concentration, you sorted by air concentration over REL. Can you through and tell us which ones you put in a different place than that order

based on the cancer data?

DR. FRIEDMAN: That's what I was asking before, and you said we should defer it --

DR. GLANTZ: Right. I know.

DR. FRIEDMAN: -- until she was done.

DR. GLANTZ: All right. I'll be quiet.

CHAIRMAN FROINES: Melanie, I'm confused about something. Your Table D has a list of 35 chemicals, and this document that Stan and Paul were just talking about has 88 on it.

And, for example, you have N-Nitrosodimethylamine, which has a cancer risk times air concentration of 1.2 times 10 to the minus 2, which is the second highest number in that order, and yet it doesn't make the list of 35. Can you say why? Because clearly if you asked the question from the point of view of carcinogenesis, it would be a high player, a significant compound. And the same with dimethyl sulfate, although, I don't believe those exposures --

DR. MARTY: Okay. The ambient air concentration data was of variable quality. We had a lot of confidence in the stuff we got from ARB. They also had data that they collected from around the U.S. primarily that we had less confidence in, and, in some cases, it was just one -- a single measurement. The

nitrosamine data, we didn't have a lot of confidence in the air concentrations. It rang bells for us for certain.

We had more confidence in some of the other chemicals from a toxicological perspective in terms of differential sensitivity, and we had more confidence in some of the other chemicals from the perspective of quality of the ambient concentration data.

CHAIRMAN FROINES: But if you have something that is -- if you have two compounds that are two orders of magnitude greater in their cancer risk than everything else, one could say why would you exclude them?

DR. MARTY: Well, the only argument you would make to include them was that you were concerned that because they were carcinogens there's automatically a differential impact in children. We are evaluating that, the issue of age and exposure and weighing potency for age and exposure, but we're not there yet. Our methods for doing that are not ready for prime time.

So we were -- while it is a factor and it is a concern. It's not necessarily enough to bump other chemicals out of the way.

DR. GLANTZ: Well, I --

CHAIRMAN FROINES: It's not clear why it

doesn't make the list of 35, which would then be 26.

DR. GLANTZ: If I just before -- can I go back one step?

CHAIRMAN FROINES: Let me just finish this because -- let me just finish this train of thought. Let me say one -- let me say two things. N-Nitrosodimethylamine is a product of oxidation of unsymmetrical dimethylhydrazine. It's found at Rocketdyne. You find it at that air force -- that Aerojet in Sacramento. It is a product of places where hydrazines have been used. So we know it exists in California, at least as a residual from those past uses.

There are probably 2,000 papers in the literature on the carcinogenicity of dimethylnitrosamine, so that you have an enormous database. You actually have evidence of exposure. So it seems to me that -- I don't understand how you could then say, "We don't want this on our list of 35 to evaluate." I mean, there is probably no compound that has as many publications on carcinogenicity as that particular compound.

So one could look at it from the standpoint of differential susceptibility. So it doesn't make any -- I don't understand it, and I raise it only because the issue of everybody's understanding of why things are

where they are is really important as everybody has been saying.

DR. ATKINSON: It's largely there, I assume, because -- in that position in that table because of the ambient air concentration data concentrated points.

DR. MARTY: That's the problem.

DR. ATKINSON: It looks sort of high to me.

CHAIRMAN FROINES: It's very high.

DR. ATKINSON: This stuff photolyzes with a lifetime of about 5 minutes, so here in the daytime you wouldn't expect it.

DR. MARTY: That's precisely the problem we had. We had not very much confidence in that ambient air concentration data.

DR. BLANC: But, again, doesn't your statute address potential air exposure as well as measured air exposure? And, therefore, isn't the technology --

DR. MARTY: What it says is "consider public exposures to the toxic air contaminants." I don't think it's prescriptive in how you do that.

DR. BLANC: But you have interpreted it as being prescriptive because you said if we don't --

DR. MARTY: Not really.

DR. BLANC: Haven't you said if we don't have air monitoring level data showing it's there, or we

don't have toxic inventory release data, even though we have reason to believe from other logical analyses that it is there, that --

DR. MARTY: We have started with the best data available, which is the ambient air concentration data from ARB. We added in other data that we had, some of it of varying quality. We looked at the emissions inventories from stationary and mobile sources. All of those things fed into the decision of whether or not there's exposure and whether the exposure is significant. It's not a process that is without flaws.

CHAIRMAN FROINES: I think the problem -- I think the generic problem -- and this happens at EPA. It happens with all agencies that deal with regulation as well as science, and that is that they tend to chase their tails. They tend to pursue chemicals that are regulated, and then they pursue those chemicals further then they pursue those chemicals further and N-Nitrosodimethylamine never gets into the loop because it's not a regulated chemical.

So the problem is that you keep looking at the same compounds repeatedly. And I think the danger is that there needs to be a way in which other chemicals can enter into the evaluation process because they may represent problems that are as yet unidentified or

having not been pursued.

And I think that's what Paul's raising about the manganese question because I think -- Roger is right. N-Nitrosodimethylamine is probably a problem at Edwards Air Force Base and Aerojet and at Rocketdyne, but it's not a problem anyplace else. It is a historical problem from the use of a particular hydrazine, but it still has 2,000 papers on its carcinogenicity.

And so if it can never make its way into the process, then we never think about it. We keep looking at the ones we already know are problems, and manganese is another example of that kind of issue.

DR. ATKINSON: But I thought it was also in the cigarette smoke, the --

MS. REPORTER: I'm sorry. Could you speak into the microphone?

DR. ATKINSON: -- N-Nitrosodimethylamine.

CHAIRMAN FROINES: Absolutely. In fact, they're in large quantities.

DR. ATKINSON: Also the exposure.

CHAIRMAN FROINES: Yeah. That's right. And I don't know about nitrosamines from diesel, do you?

DR. ATKINSON: What?

CHAIRMAN FROINES: Do you know about

nitrosamines from diesel or gasoline?

DR. ATKINSON: I shouldn't -- I wouldn't expect to find them. The other place you might find them is from cattle feedlots.

CHAIRMAN FROINES: Um-hmm.

DR. ATKINSON: Oxidation of a means.

DR. BLANC: Melanie, can I ask another clarification of methods?

DR. MARTY: Sure.

DR. BLANC: So going from Table C to Table B and then to -- from Table B to Table C -- I'm sorry -- and then from Table C to your list of 35, when there are --

DR. MARTY: That's the next slide.

DR. BLANC: Yeah. On -- it's just a methods question. On Table C, there are, in fact, pesticidal chemicals, so the exclusion of pesticides occurred at a later stage for some, or are these pesticides for which the ARB has already --

DR. MARTY: It was really when we were going from the 95 to picking which ones we wanted to do focus literature reviews on that we realized we couldn't look at pesticides in their pesticidal use.

Now, acrolein is used as an herbicide, but it's also a product of incomplete combustion.

DR. BLANC: Right.

DR. MARTY: So looking at acrolein --

DR. BLANC: Was okay.

DR. MARTY: -- was okay.

DR. BLANC: So going back to my earlier question about parathion, which was really a question about organophosphates, were there no organophosphates at all that made it to Table C therefore? And obviously not -- and that would only be on an exposure reason because you had not yet --

DR. MARTY: Yes. That's right. It would be on the exposure reason.

DR. BLANC: So the only ones for which there were no organophosphates already listed as TACs for which there would be any ambient exposure to any one of them because clearly you would have to consider the combined effects?

DR. MARTY: Could you -- I'm not sure what you're asking.

DR. BLANC: I'm asking again for transparency. Let's say I'm reading this down the line, and I get to Table C, and then I -- and then there's a footnote, not there currently, which says, "This list includes pesticidal chemicals with TACs that are pesticides and have no other use whatsoever; and, therefore, the ARB is

excluded from regulating them, and the statute excludes us from looking at them. And so at this point, although we would have looked at them, if we could have from a scientific point of view, from a regulatory point of view we're prohibited."

DR. MARTY: We could put that footnote in.

DR. BLANC: I would put it there in caps and bold.

DR. MARTY: I don't think it's that simple.

DR. BLANC: Why isn't it that simple?

DR. MARTY: Because we still aren't at the point where we have scientific evidence for children, either on an individual basis or population-wide basis, being impacted more than adults. So while that's true and we can put that footnote in, it's just one piece of the puzzle. It's not the whole reason, perhaps, that certain things were not looked at.

In the case of pesticides, we really can't --

DR. BLANC: I'm talking about -- okay. I'm talking about acetylcholinesterase inhibitors.

DR. MARTY: Inhibitors. There's not much we can do because of the way the statute is written.

DR. BLANC: I understand that, but let's say you didn't have that statutory prohibition. Just as a scientist and a public health regulator, wouldn't you

have been very interested in organophosphates or any acetylcholinesterase inhibitors because of previous discussions in terms of pediatric issues in acetylcholinesterase functions?

DR. MARTY: Yes.

DR. BLANC: So from a scientific point of view, wouldn't anything that was an acetylcholinesterase inhibitor have been of particular interest in this process had it not been specifically prohibited from you looking at it?

DR. MARTY: We would have been interested in it, yes. I --

DR. BLANC: Okay.

DR. MARTY: You folks had a presentation on OPs, and the potential for differential impacts comes up when you're looking at tyrosinase, for example.

DR. BLANC: So don't you think that one potential utility of your document in terms of public health protection would be to highlight areas for which the science will direct you to look but for which your hands are tied from a regulatory point of view?

DR. MARTY: We could put that in there. Yes.

CHAIRMAN FROINES: I think it's -- I think what Paul is raising is that this is an extremely important document, and if one views it narrowly, one comes out

with a list of five chemicals. And I think, for the record, for OEHHA to be on record of defining the breadth of the issues is really very important because it forms the basis for subsequent legislation or activities that might take you to another level of investigation.

DR. MARTY: The light just came on. I'm sorry. Yes. If you're viewing a document as not with my brain but a brain of an outsider, you would want to know why pesticides weren't in there.

DR. BLANC: Well, I'm speaking now specifically about organophosphates. We could discuss organochlorine compounds separately, and I think the science is probably more complicated.

DR. MARTY: Yes.

DR. BLANC: But --

DR. MARTY: This document has many audiences, in other words.

DR. GLANTZ: Well, can I --

CHAIRMAN FROINES: Yeah, Stan. We cut him off.

DR. GLANTZ: I'd like to go back to Gary's question now, which now we've reached the precisely right time to ask. If you look at table -- I'm just trying to understand and get on the record exactly what you did. And so we have Table 1, which is a list --

which is what? That's list C; right? No.

DR. MARTY: List C is the 95 --

DR. GLANTZ: Okay.

DR. MARTY: -- TACs for which there are --

DR. GLANTZ: Okay. And that's what ends up in Table 1; right?

DR. MARTY: Pretty much with a few exceptions where we couldn't rank them because we didn't have --

DR. GLANTZ: Okay. So while Paul was talking, I went through Table 1 and --

DR. BLANC: You mean you weren't listening to me?

DR. GLANTZ: I was listening. I can do two things at once.

Anyway, I just went through Table 1, and you're right. For the most part things are ranked by the air concentration over the REL. But let's just go down to ones that aren't, and you can just briefly tell us why you put them where you put them; okay? I can tell you it's No. 6, 7, 10, 21, 31, 32 and 33, 41 and 42, 46, 58, and then there's all the stuff at the bottom.

So I think it would be instructive just if you could briefly just tell us -- because all the ones that are ranked by the RELs, that's obvious what you did. So if you could just go down and say why did you put, you

know, the things where you put them on the list.

DR. MARTY: Okay. We can do that, but I want to caveat it by saying that this breaking has limited utility in coming up with five TACs that may cause infants and children to be especially susceptible.

DR. GLANTZ: Okay. We're just trying to understand the process.

CHAIRMAN FROINES: I don't think you should go through that entire list.

DR. GLANTZ: Okay.

CHAIRMAN FROINES: I think if Stan wants more, he can ask for more, but let's do it -- I'm worried that we probably should --

DR. MARTY: Okay.

CHAIRMAN FROINES: -- get to the chemicals after lunch, so that between now and lunch we want to deal with the methodology which gives us about an hour to do that.

DR. FRIEDMAN: How about No. 21?

DR. MARTY: Okay. But --

DR. FRIEDMAN: Which, you know --

DR. GLANTZ: Pick a couple. I'd like to hear about a couple.

DR. MARTY: For one thing, No. 10, betadine made the final cut for us to look at differential

impacts. So where it is with respect to 8 times 10 minus 5 being a bigger number than 2 times 10 minus 5 doesn't really matter in the final analysis. We stuck it on the list of 35.

DR. GLANTZ: Okay.

DR. MARTY: Dimethyl sulfate and dimethylane --

DR. GLANTZ: Wait. Wait. Wait. But with butadiene -- so you're saying that -- so tell me again why? I'm just trying to go through the process. So why did you put it where you did? And I realize in the end the lists end up back to being alphabetical. But why? It ended up pretty high on the list, you know. I'm not asking, like, why is it No. 10 instead of No. 9 or No. 11, but why did you push it up? Because if you look at the REL, it would have been way down. It would have been like 20, 25 or something.

DR. MARTY: Right.

DR. GLANTZ: So why did you put it about where you put it?

DR. MARTY: Because of the potential for carcinogenicity and widespread exposure.

DR. GLANTZ: And then what about -- you talked about No. 7; right? That was what John was talking about.

DR. MARTY: Yes. And dimethyl sulfate falls in

there also.

DR. GLANTZ: Okay.

DR. MARTY: We were pretty unsure of those ambient concentrations in that. I probably should have just taken them out entirely, but I didn't.

DR. GLANTZ: Well, but no. But I'm asking -- so you -- those -- if you look at the cancer risk as computed, those are like really huge numbers, so that's why you pushed those up there. Okay. And then Gary had asked about chromium.

DR. FRIEDMAN: You base that on the cancer number it looks like.

DR. MARTY: Yes.

DR. GLANTZ: Why did you put it where you did in the -- because all the other cancer numbers on there were like 10 to the minus 5, is that why you put that there?

DR. MARTY: Right.

DR. GLANTZ: But then if you go down to, like, 31, 32, 33 you've got a bunch of, like, 10 to the minus 5 cancer numbers. How come you didn't put those higher?

DR. MARTY: We weren't particularly concerned about chlordane and heptachlor which are banned pesticides. And tetrachloroethane, I can't remember why we didn't move it up. For one thing, it's a Class 3

carcinogen, an IARC 3, on the U.S. EPAC, so that you'd be less worried about a 3 or a C than something like perc, which is a 2A, or something like beryllium, which is a 1.

DR. FRIEDMAN: So even though it's a lot of work, I would recommend that you just be explicit in the document about these decisions and how you arrived at it.

CHAIRMAN FROINES: Melanie, I have a question. Continuing this list of -- you know, I made the point about chemicals that get regulated get continually looked at, and chemicals that aren't don't get looked at very effectively by these processes, and I'll give you an example of one that I think is extremely important that is on this list ranked 82nd, and that is naphthalene.

And George knows that's a compound of particular interest to me for two reasons: One because the chronic (phonetic) amobioassays are positive in both rats and mice at this point. So one would probably -- even though it hasn't been necessarily ranked by international agencies like IARC, it's still one that NTP would consider a carcinogen. And I don't know what ranking it would have, but we would have to take it seriously.

And then if you look at the data that Roger and Janet developed in the -- when they were looking at PAH concentrations, it's certainly in very high concentration in California. And so how a compound of that magnitude -- of that importance ends up at 82nd is a mystery to me.

DR. MARTY: Well, it's actually -- since it's a polycyclic aromatic hydrocarbon and we decided to look into polycyclic aromatic hydrocarbons because there's a lot of information on developmental toxicity and potential or differential effects, it's actually included under the PAH.

CHAIRMAN FROINES: It's included under the PAH, and that also is something -- this is a side bar, so I won't pursue it, but it's something that worries me because
we -- this panel put a lot of time into PAHs some years ago and identified them as TACs, and there has been no single, control-strategy approach taken, even though we found it a TAC. So that in some cases I prefer that we look at individual compounds to try and drive the system to some extent because that's out of the risk assessment mandate for this panel.

But the point is that sometimes it's useful to look at chemicals and not simply lump them because

lumping them may end up the fact that they get lost in the shuffle if we're not careful. And naphthalene I think is a chemical that definitely should not be lost in the shuffle.

DR. MARTY: The only thing I can say is that PAHs are again being evaluated under the TAC program. ARB has requested us to review the information on PAHs, naphthalene among them. So it will be addressed through that program.

DR. BLANC: So in terms of on the table that this relative ranking which then derives very closely to the ones that -- the 35 that end up on Table D is closely driven by this table with certain exceptions. This has a big impact. Again, these are questions trying to understand the process you used. So somehow table -- this table --

DR. MARTY: Could we have the next slide, and I can talk about that? It is -- it does drive it somewhat.

DR. BLANC: It is one of the factors.

DR. MARTY: It's one of the factors.

DR. BLANC: So that if something --

DR. MARTY: But the disconnect comes in. If you just look at the top 50 or 60 by rank, you may not be picking up chemicals for which you know there's a

differential impact.

DR. BLANC: Right. And then things that didn't appear on the table were all -- weren't necessarily excluded?

DR. MARTY: Right.

DR. BLANC: And those are some eight in number?

DR. MARTY: Right.

DR. BLANC: And those don't appear here because you don't have the draft or an adopted REL example? Is that an absolute reason?

DR. MARTY: It's primarily because we didn't have good ambient concentration data to use in the ranking.

DR. BLANC: Well, you have lots of things without ambient concentration data here.

DR. MARTY: Right.

DR. ATKINSON: In fact, it looks to me as though that would have been somewhere to put a fair amount of effort into, going through the literature and trying to find out at least some idea. Admittedly, it's going to be time and place dependent, but at least get some idea of what sort of concentrations are out there and ambient.

DR. BLANC: So it can't be --

DR. MARTY: We did do that --

DR. ATKINSON: That's what drives the whole thing.

DR. MARTY: We did do that for certain chemicals that we had concerns about, but we could not possibly do that for all 200 chemicals given the time frame.

DR. BLANC: No. But, Melanie, I'm just trying to understand this. I mean, half of these don't have air concentrations to REL levels --

DR. MARTY: Okay.

DR. BLANC: So that can't be the reason why some of these aren't on that table.

DR. ATKINSON: Especially those with --

DR. MARTY: Okay.

DR. ATKINSON: -- small RELs.

DR. MARTY: Your first assumption was correct. Dave is correcting me. It's because they didn't have health criteria, either a developed REL or being a risk factor. In one case --

DR. BLANC: Either draft or --

DR. MARTY: In one case, which I need to get on the record, lead was initially going to be dealt with under SB 25 in the criteria air pollutant process, which is a separate process. It was decided that they weren't going to deal with it under the criteria pollutant

process. They wanted me to deal with it under the toxic air contaminant portion of the statute. So lead is -- gets added in partway through the process.

DR. BLANC: And the other ones are for which there's neither a draft nor an accepted REL?

DR. MARTY: Yes. Staff is saying yes.

DR. BLANC: Can you list those so that they're in the transcript?

DR. MARTY: Those were the ones that I went through a few minutes ago. Okay. It's -- MEK was one and CS2 was one, but some of these others, it must have been -- it must have been the concentration data that made us add it back in.

These are the ones that have ambient data. He's asking for ones that didn't have RELs. We've just got to go back and list out which ones had RELs and which ones didn't have RELs. I can't do it right here.

DR. GLANTZ: Let me ask a question. Are you having fun now?

DR. MARTY: No.

DR. GLANTZ: Okay. If you go down to No. 59 in the last part of the list, those are the ones where there's like nothing in the last two columns of the paper. Okay. Do you have anything that you just want to say about that? Is there any comment, you know, to

explain sort of -- how did they even get into this table, if there's, like, nothing there? For those, there's no ambient -- I guess are those ones where there's no ambient air concentration data, but you think they're bad?

DR. MARTY: And we had emissions inventory data.

DR. GLANTZ: I see.

DR. ATKINSON: I mean, I'll just take one example, ammonia, which is 64. It's got this rather large REL of 200, but if you go out to Mira Loma where ARB conducted a study two or three years ago, they were seeing up to 700 ppb out of the feedlots. So even with a huge REL like that, you can still end up with a fairly decent-sized number regarding the air concentration amount.

DR. MARTY: Okay. Fifty-nine on, there's no ambient data, but there were tox data.

Ammonia is on the 95 TACs that we chose a portion of to do focus literature searches. One of the reasons is there's -- obviously, there's a lot of exposure to ammonia. It's used tremendously. There's huge emissions from stationary source.

DR. GLANTZ: Okay. Well, then -- so the next question and then you could put your next slide up.

We'll try to keep your frustration --

DR. MARTY: Go back.

DR. GLANTZ: To the next slide. That's the one.

DR. MARTY: This is going from the 95 to the 35.

DR. GLANTZ: Okay. Now, I want to ask a question about that.

DR. MARTY: Can I go through the slide first.

DR. GLANTZ: Okay.

CHAIRMAN FROINES: Go ahead.

DR. GLANTZ: Go to the next slide.

DR. MARTY: Because we had limited resources and time, the deadline of the statute, we couldn't possibly do a focus literature search on all 95, so we decided to take about a third of them and look at about a third of them.

We focused on some that had -- that ranked high because of the REL and the ambient, for example, acrolein. We focused on some that ranked high because of the carcinogenicity hoping to find something that may shed light on whether there was differential sensitivity.

But we also ended up weighting those with known toxicological properties that have been shown or might be expected to demonstrate differential sensitivity in

young persons or mature animals.

For example, lead and mercury are well-known developmental toxicants. Despite the fact that there aren't huge exposures on a regional basis, we had concern of those -- over those for the toxicology information and the epidemiology information that's out there, and there actually are hot spots facility emissions of those two chemicals out there.

DR. GLANTZ: Okay. I think that's all sensible. The technical question I have -- and, again, this is just trying to get everything out there on the record. It's not that I think you're a bad person.

So if you take the 95, if you take Table 1, which has a ranking that we now more or less understand, how does Table C -- if you took the top 35 compounds on Table 1, okay, and you're saying to us, for reasons which I personally think are quite reasonable, that you didn't slavishly follow this list, how did -- what is there on Table C which is different from the top 35 -- or not Table C.

DR. MARTY: Table D has the --

DR. GLANTZ: Table D. I'm sorry. What is there on Table D that is different from the top 35 chemicals on Table 1 and why? If you could just go through and explain to us those that were added or

deleted from the top 35 of Table 1. You've already dealt with a couple of them.

DR. MARTY: Okay. Acrolein is No. 1, so that made the cut. Acetaldehyde, it made the cut, and we're concerned about the toxicity.

DR. GLANTZ: Okay. I'm just asking you just the narrow question.

DR. MARTY: Okay.

DR. GLANTZ: If you take the top 35 in Table 1; okay? What is there in Table D that isn't in the top 35 of Table 1, and why did you add it and then --

DR. MARTY: Okay. Asbestos got added in because of concerns about long latency and shelf life of kids. People who are exposed early in life to asbestos end up with mesothelioma in their thirties and forties.

DR. GLANTZ: Okay.

DR. MARTY: So that was a concern.

Okay. I'm going from -- George is confusing me. I'm going to try to talk about the things that weren't in the top 35 that by this scoring -- they end up in the top 35 on this scoring.

DR. GLANTZ: Yes. That's right

CHAIRMAN FROINES: I think that -- I think that -- I think one has to establish criteria at each level as a basis for the decision making and then that

drives how you then do it.

DR. MARTY: The --

CHAIRMAN FROINES: So I think that we don't need to go through 35 different chemicals right now. I think we need to describe what is the basis for the differences between the first 35 in one table and the next 35 in another.

DR. GLANTZ: And I think that-- no. Well, I disagree with you. I don't think we need to go through all 35, but I think Melanie has explained the criteria. I'd just like her to very briefly just explain to us the ones where they don't match up. So asbestos is one, and there aren't that many of them.

DR. MARTY: Vinyl chloride is another. There's not a lot of exposure on a regional-wide basis. There are some concerns about hot spots exposures, for example, measurable vinyl chloride levels near landfills. So that's another reason. But if you look at the toxicity piece, it's clearly more potent when exposures occur either in utero or perinatally. So to us, that was an important thing to get out and discuss in this document.

DR. GLANTZ: Okay. What else? You already mentioned lead and mercury.

DR. ATKINSON: Looks like dioxins.

DR. MARTY: Dioxins is another example where there's a lot of toxicity information that indicate differential effects. There's a lot of concern about low level exposures to dioxins at current ambient levels of exposure, and that's from all routes of exposure.

DR. ATKINSON: 1, 4-Dichlorobenzene, No. 40

DR. GLANTZ: And why was that?

DR. MARTY: I have to get back to you on that one. I can't remember why we moved it up.

DR. ATKINSON: Well, that may be because the pesticides fell out; right, things like chlordane and heptachlor? So that would mean that the top 35 on List D would have been the top 40 on List 1.

DR. MARTY: Yes.

DR. GLANTZ: So, basically, then -- so you dropped out the pesticides, and then there are these one, two, three, four, five, six you just discussed, and everything else then would be in the top Tier on Table 1; is that correct?

DR. BLANC: No. Carbon disulfide doesn't appear on Table 1 because they didn't have a draft for an accepted REL; is that correct?

DR. MARTY: Yes.

DR. GLANTZ: And then --

DR. BLANC: Lead wasn't there.

DR. MARTY: We were concerned about the neuro-toxicant.

DR. GLANTZ: Okay. And then lead -- you already talked about lead and mercury. Any others?

DR. MARTY: I'm remembering that we moved benzopyrene up and actually the whole class of PHs, and that again is driven by the information on the toxicology of those compounds. It will be hard to ignore that information because the exposures are lower.

DR. GLANTZ: There's lots of that in cigarette smoke, too, actually.

CHAIRMAN FROINES: Well, I think we can --

DR. MARTY: The other issue is that --

CHAIRMAN FROINES: I really think this is not -- that this reaches a level of usefulness. The ultimate document has to describe the basis for decision making so that everybody understands it. We don't need to go through each one.

DR. GLANTZ: No. I think we've gotten this adequately, and I think the reason that you're presenting is all very fine.

But as John just said, I think this needs to be spelled out in the document, and then I think nobody can say, as several of the commenters said, "We don't understand how you got the list." And I think people --

as somebody said, people can argue with you about the judgment that was applied in getting the list and that's their prerogative, but I think -- I think we have to make it very, very clear how you ended up with this.

I think, again, from my meeting with Melanie and her staff and what's been said today, I think they employed reasonable criteria. I just think that they were absolutely not explained, and I think that's what's caused a lot of the difficulty.

So, anyway, so then you ended up with Table B. Okay. And then we will now allow you to show one more slide. So you did the focus literature reviews on all 35?

DR. MARTY: Yes. And some of them we have very recently done the literature reviews.

DR. BLANC: Did you out source this?

DR. MARTY: Yes.

DR. BLANC: And is that -- that wasn't really stated very explicitly in the document.

DR. GLANTZ: Well, they do that all the time, though. I don't think that's an issue.

DR. BLANC: I think that is an issue because I think that it could come back to be an issue, and I think that transparency is very key. And there's certainly nothing to be embarrassed about if you out

sourced it to, you know, reputable, you know, academic bases, professional members.

DR. MARTY: We out sourced it to UCB, UCLA, USC. What else? UCSF.

DR. FRIEDMAN: What did you out source? The literature review and the summaries of the literature?

DR. MARTY: Right. We contracted the reviews of most of the 35 out. Some of them were done in house.

DR. FRIEDMAN: But not the decision making. Just the information gathering.

DR. MARTY: No. Just to get the information, pull up the -- get us the papers, a summary of the papers, then staff then took that information, read the papers, decided whether we agreed or not with the contractors, which in some cases we did not, and then put the document together, choosing just those 11 that we thought had the strongest information based on the focus literature reviews.

DR. FRIEDMAN: I agree with Paul. I think that's really helpful to know that, and it again does not detract from your process.

DR. MARTY: Okay. We've never really put into a document before whether we've contracted out or not.

DR. GLANTZ: I think that I actually don't agree because I think that the document is OEHHA's

document, and I think they're the ones who are responsible for what it says. And if they hired someone to assist them in preparing it, then I don't see how that's relevant.

DR. BLANC: I'll give you an example of how I think it's relevant.

DR. GLANTZ: Okay.

DR. BLANC: I think it's relevant because if you farmed out five chemicals to some whose area of particular expertise was carcinogenesis, and you farmed out five others to somebody whose area of research is neurotoxicology, and those are chemicals both -- and you very wisely put the five out that you have reason to believe to act as neurotoxicants to researchers with expertise in that area, that strengthens the conclusions that you eventually drew. Unless, for some reason, you have trepidations about how you did the out sourcing, it would seem to be strength, not a weakness.

CHAIRMAN FROINES: I also think, quite frankly, I agree with Paul. I'm on the Board of Scientific Council of the National Toxicology Program, and all the documents we get for review list the contracting agencies that did the documents for NTP. So I think for consistency it would be wise.

But also, I hate to say this, but some of those

documents that they have contracted for turn out not to be very well done, and I think that the Board of Scientific Council raises questions about the quality of the documents. And so it seems to me that it's better to have it all laid out on the table than to not have it laid out. I think everybody needs to be able to understand what went on in a process so that we can improve the process. It's not --

DR. MARTY: We can put it in. We can put it in.

DR. GLANTZ: Okay. I think the thing, though, that's important to stress, though, I relent, but I think the important thing to stress though is that they may maintain someone on the outside to draft something for them and collect information for them, but it's their document, and I consider OEHHA to be the authors of the document, even if they hire somebody to draft something, because it is their -- I am assuming that if something comes forward, it's OEHHA speaking, not some contractor that they happened to hire. And I think Melanie said that, that they took the material and then they applied their professional judgment to what was then forwarded to us.

DR. BLANC: That wasn't my implication.

DR. GLANTZ: Okay.

CHAIRMAN FROINES: But I think that the role as envisioned by the legislature, this panel is a kind of quality control. That's why we review what you do, and, therefore, the more information we have about how you do what you do, the better off we can fullfil our responsibility.

I have a question. I think we could use a five-minute break for the court reporter. We're also 25 minutes or so from -- how long do you think you're going to go on, Melanie? I realize -- I realize that's a very open-ended question.

DR. MARTY: Okay. I'm just looking at --

DR. GLANTZ: She has one more slide. Three hours.

DR. MARTY: I have nine more slides. On the process I only have, basically, two more slides, and then I wanted to talk a little bit about one of the endpoints that we chose as the basis for some of our decisions and why we chose it.

CHAIRMAN FROINES: That's a very, very good answer, and so we'll take a five-minute break for -- because closure is not within the --

DR. MARTY: Five minutes.

CHAIRMAN FROINES: -- immediate future.

(Recess.)

CHAIRMAN FROINES: Let's begin again.

DR. MARTY: Andy, can I have the next slide?

CHAIRMAN FROINES: Wait, Melanie. I don't think we have everybody seated.

DR. BLANC: Here's Stan.

CHAIRMAN FROINES: Okay.

DR. MARTY: Okay. This slide points to the criteria which we discussed in the document related to what we were looking for in the focus literature reviews of the 35 chemicals that we looked at. And the primary thing was evidence indicating infants or children may be more susceptible to the toxicity of that compound and the strength of that evidence.

We also looked at nature and severity of the effect. Particularly, is it an irreversible effect? Is it something, for example, an eye irritation versus a developmental defect? You would want to consider that.

We also looked at evidence that the existing health criteria may be inadequate. Although, this didn't play a large role in the final decision. And by that I mean whether the existing reference exposure levels for cancer potency factors would have adequately protected children.

We also looked for potential difference in susceptible to carcinogenesis based on either known or

plausible mechanisms.

We looked at the extent of exposure and/or the magnitude of risk at ambient concentrations and indications that infants and children might be more heavily exposed to the materials, particularly, for example, by deposition onto surfaces, which would occur in the case of PAHs and others, dioxins, and that really cuts to the issue of hand-to-mouth behavior in kids.

Next. We chose 11 chemicals or chemical classes for potential candidates for listing based on the information in the focus literature reviews. We weighted heavily the known toxicological properties in the compound. We weighted the extent of exposure, strongly weighted evidence for differential toxicity. Evidence of widespread exposure was also weighted and then we -- within the 11, we propose a Tier 1 which consisted of 5 chemicals for listing under the statute.

CHAIRMAN FROINES: There are two kinds of exposures. There are exposures, for example, in the ambient environment that are of consequence, and there are differential exposure, namely, that a child who has more outdoor time or what have you may have a differential exposure. And so the extent of exposure is really two categories, not one. So can you speak to that issue?

DR. MARTY: Yes. There -- if you look at something that has widespread exposure in terms of regional, on a regional basis, PAHs or benzene, about all you can say from the existing information is that kids breathe more per unit body weight than adults. They eat more, they drink more per unit body weight than adults. So for those routes of exposures, kids will be exposed to larger amounts of chemicals than adults given everything else being equal. So in the same environment.

CHAIRMAN FROINES: But things aren't equal.

DR. MARTY: Right.

CHAIRMAN FROINES: That's very important that things are not equal.

DR. MARTY: That's right.

CHAIRMAN FROINES: So there has to be a demonstration of differential exposure.

DR. MARTY: Well, what I just said doesn't help you very much to figure out which chemicals are more important from an aspect of differential exposure because, essentially, kids will be more exposed to everything, so it doesn't help you differentiate. We did try to find some information --

CHAIRMAN FROINES: That's not really true. An adult who drives two hours a day on the freeway behind a

diesel truck is going to have --

DR. MARTY: Yes.

CHAIRMAN FROINES: -- a higher exposure than children playing in the yard.

DR. MARTY: I agree with that. What I meant is given the same environment, if you stick them in a chamber, the kids are going to breathe more. Give everybody -- so within the same -- that's why it doesn't help you very much to figure out what differential exposures there are.

There's -- there are some data that can help you, for example, time activity patterns to look at how much time a kid spends in the car versus how much time an adult spends in the car and so forth. Those types of analyses are pretty time consuming and long, and we did not do that for this initial prioritization.

We did, however, look for information in the literature searches that brought those issues forward. So, for example, there's some information for PAHs that kids are more exposed to PAHs. There's lots of information that kids are more exposed to lead, primarily from hand-to-mouth behaviors.

So you are right. There's sort of the generic, yes, you have ambient concentration data. That means people are exposed. And then there's the more specific

exposure differences that are based primarily on time activity patterns and behavior.

CHAIRMAN FROINES: So that means that the fact that children have higher breathing rates and all those other physiologic factors that you lay out in your document, they were not used as a basis for defining the chemicals that are on the lists in this document?

DR. MARTY: They really couldn't be used. All you can say from that is kids have higher exposures to everything. You can't say kids have higher exposures to -- in the same environment, kids have higher exposures, but you couldn't really use it to say one way or the other unless you had specific information, like for lead, for example, or for other chemicals where hand to mouth is an important issue.

CHAIRMAN FROINES: But my point here is -- Stan, I'll get to you in a second.

My point is that you make -- in pages 3 through 9, you emphasize those physiologic differences, and the problem in the document is that you then don't use that area of emphasis for decision making. But it's never made clear in the document that the differential exposure based on physiologic characteristics was not used for decision making, and I think that that's a problem because of the nature of your emphasis when you

set out the differences between kids and adults.

So that you set it out, and then there's an expectation on the part of the reader that it's going to be used as a decision making basis, and then you don't use it. And so that creates a problem for somebody trying to read the document. It's hard to figure out -- it's hard to figure out what, in fact -- you know, who's on first kind of.

DR. MARTY: Okay. You know, we did develop that section on factors influencing why infants and children might be more susceptible than adults, and the whole purpose of that was to give a broad overview of the types of factors that influence response to toxicants. One of those is how much you're exposed. So that's the reason while all that whole section is in there.

It wasn't really meant to be applied to each specific case in the back, but, you know, obviously that wasn't clear, so we can just try to describe that a little better.

DR. FRIEDMAN: Excuse me. Didn't you use a difference like that, though, in selecting certain chemicals in relation to asthma because of children having smaller airways which are more easily blocked?

DR. MARTY: Yes. For -- yes, that's correct.

For physiologic differences. And, of course, there's -- I shouldn't say we didn't -- I shouldn't say we didn't use them. That's not correct either. Certain things applied in some of those chemicals. A lot of them didn't, but it doesn't mean we didn't consider it or think about it when we were going over one choice or the other.

CHAIRMAN FROINES: But Gary's asking it -- Gary's asking a question which is very bothersome to me, which is he's asking the question in a generic way. And yes, of course, it's a given in a generic context that's true. Children have smaller airways, therefore -- but that doesn't mean that you then have any evidentiary basis to show differential exposure.

DR. FRIEDMAN: Well, I guess what I was saying is that we sort of came down with a blanket statement that the material on 3 to 9 was not used at all. These characteristics of children as comparison in adults was not used at all in making the selection of prioritization. What I was saying is that I think some factors, particularly the narrowness of the airways, this is an exception that that was used. That was the point I was trying to make.

DR. ALEXEEFF: I think the point of -- George Alexeeff of OEHHA. The point of the first section, we

did try to consider those factors. For example, on the breathing rate information that -- a lot of -- most of that information was in the CCAA document that we had on exposures where we looked at activity patterns of children and adults and built the exposure differences.

So we tried to look at that information to see if it could be applied, and I guess there were specific cases, as you mentioned, where we found some concerns. Just asthma we looked at more carefully to see if there was an issue that played out with the chemicals.

But some of the issues that Melanie pointed out, for example, the overall breathing, breathing per kilogram, okay, that was a factor that, in general, children -- their whole distribution is -- indicates, in general, they breathe more per kilogram body weight than adults. So that wasn't a way of differentially choosing any chemical.

We thought about -- we thought about it many ways. You know, maybe we can look at particulates or gaseous chemicals, but we couldn't come up with something. What we could do is we could possibly add to those sections whether or not that section led us to something -- to a conclusion to list chemicals or to identify chemicals or whether or not it was just a general factor that we just, you know, sort of felt

might apply to all chemicals but not differentially to every chemical.

DR. FRIEDMAN: That would be very helpful to add statements like that.

CHAIRMAN FROINES: Stan.

DR. GLANTZ: I had a couple questions. I'm still trying to get from Table D to 11. Poor Melanie. The first question I have, which is just reflecting my own ignorance, is in Table 1 of the document where you list the 11, you have non-coplanar PCBs, and I don't see that on Table D, or is that just they're called something else?

DR. ATKINSON: They're coplanar PCBs.

DR. GLANTZ: Well, coplanar PCBs are in, but they also list in Tier 2 "non-coplanar PCBs."

DR. MARTY: I'm looking for Table D. We had lumped dioxins and PCBs together, and we should have put coplanar and non-coplanar PCBs in that table.

DR. GLANTZ: That's two separate entries.

DR. MARTY: Right. This is the list of the compounds that got literature reviews. It shouldn't just say "coplanar PCBs" because we were looking at PCBs generally. So if you scratched out the word "coplanar" --

DR. GLANTZ: Okay. I think it would be -- this

is just, again, making it totally transparent, since you ended up treating them differently in the report, I would suggest you have 36 things in --

DR. MARTY: Okay.

DR. GLANTZ: -- Table D. That way it's all -- and the other -- make sure all the tables kind of fit together.

Then the other question I had is if you look at the 35 or 36 compounds in Table D, you drop out 20 of them. And I have two questions, one for you and one for the panel. And, that is, does anybody disagree for the panel, that is, did they drop anything out that you think they shouldn't have dropped out?

And the question for Melanie is to just -- if there's anything more worth saying about why you dropped the 20 that you dropped to get from Table D to Table 1 in the report? So I think that -- I'd like to hear a little bit about that process with a few specifics and then see if the panel agrees.

DR. MARTY: What drove the choice of the 11 was evidence for differential effects either in children versus adults or in young, experimental animal versus mature, experimental animals.

DR. GLANTZ: Okay. So the 11 that you picked then were the 11 where you had strongest reason to think

that was the case?

DR. MARTY: Yes.

DR. BLANC: But think about it from my position, sitting here with the -- your detailed chemical substance-by-substance Appendix B of the 11 that you chose. How am I supposed to scientifically review your decision of those 11 versus the other 25? Because OEHHA said so?

I mean, from my point of view, just give me some guidance here. How am I supposed to accept the decision that manganese compounds, which made it into the 36, were excluded from the possibility of being in the 11. And that I agree with the rationale for that -- I mean, I don't think, you know, seeing 97, you know, reiterated case summaries because actually you didn't get detailed evaluations.

So you go through and you said, okay. You've explained the rationale for how you got down to 35 for which you then contracted out to have, you know, fairly detailed evaluations. I don't know whether I agree with what your -- what the --

If, for example, again to use manganese as an example, if the point is that there have been good animal studies looking at neonatal equivalent exposure and deficits with manganese and they've been negative

studies or whether the issue was that you don't feel there's been enough animal data to look at preferential neurotoxicology and the developing nervous system of the appropriate animal model, I mean that to me would have a very -- those are two very different scenarios; right?

I realize that with -- particularly with the organified manganese, the data are only emerging now and are quite limited. But clearly it's a huge, huge, huge public health issue. And I would want to know exactly what the basis was for excluding it.

Similarly, carbon disulfide, very large air emissions, very important neurotoxin, very important vascular toxin, very important peripheral known toxin. What is the basis for which that fell out? Is it because you couldn't find an animal study in the literature, or there are ten animal studies all of which are negative for differential effect?

DR. MARTY: Primarily, it's because of the lack of data to describe a differential effect.

DR. BLANC: And in those situations, did you have a clear policy for when you would -- so you have this policy that you've taken, which we haven't got to yet, on asthma, and, ipso facto, the airways are narrower; therefore, anything that is an irritant you will assume has a preferential effect, and maybe you

have one sort of semi-study of secondary data analysis of, you know, a cohort from Arizona that suggests that kids have peak flow in environments where one of the things that was measured was formaldehyde.

But you've got this -- it's very heavily driven by the assumption which you're about to get to in the following slides about asthma. But I could make certainly the same assumptions about anything which is a neurotoxin that affects, preferentially, areas of the nervous system even if I don't have great animal data showing that pups are going to do worse than, you know, six-month-old animals.

DR. MARTY: Well, maybe I should flip the question back. If you have strong evidence, you have the studies that show in pups neurotoxicity for chemical X but for neurotoxin Y you don't have that information, to us, the fact that you had specific studies was a stronger indication of a differential effect than the general assumption, which lots of people make that neurotoxins are going to be worse in young animals.

DR. BLANC: But your review of your substances made it by being neurotoxins. In fact, the only one in the top five is lead and mercury on the bottom. Those are the --

DR. MARTY: Okay. Then what the difference --

what we have to factor in is exposure. So where we had strong evidence of exposure, then that also propelled something higher up in the chain.

For mercury, there's lots of exposure, but it's mostly from fish or water borne pathways in California. There are some hot spots of exposure in terms of airborne.

DR. BLANC: Okay. But I'm not arguing about mercury. Mercury made it into the 11. I'm talking about the things that didn't even make it into the 11. They're not even on the radar screen anymore.

DR. MARTY: That was primarily a lack of direct studies looking at --

DR. BLANC: Rather than studies that were done that were negative?

DR. MARTY: Yeah.

DR. BLANC: And that's a big difference, isn't it, from a public health point of view? So these are chemicals which are presumed innocent until proven guilty.

DR. MARTY: Yes. But it comes back to we have to pick five.

DR. BLANC: I understand you have to pick five, but first --

DR. MARTY: So which five are we going to pick?

The ones that are presumed innocent until guilty?

DR. BLANC: Well, I don't know. I can sit here and make the argument that I think neurotoxicity would drive things a hundred times more than the issue of whether an irritant would cause airways to be narrower in children. And I could also make the argument, and I just may be a little out of order, but I know that you weighted things towards developmental -- prenatal developmental effects drove some of these things.

DR. MARTY: Actually, most of it's postnatal. Some prenatal.

DR. BLANC: Some prenatal.

DR. MARTY: You're right. You know, from a scientist, you have to worry about both in utero and postnatal. But I understand your point, and you can see how hard it was for us to do this.

DR. BLANC: I understand. But I can't see -- because we're talking about it, but I can't see from the document.

DR. GLANTZ: I think the question I would ask to you is you prepared these 35 reviews -- or I would say 36 since you split the PCBs into two groups. I mean, is there any reason that you couldn't in the next iteration of this document include those or have an appendix document or something so people can see what

there is to see? You know?

And then I think -- I think that if that wouldn't be like a horrible, onerous thing to do, I think that would help. And then I think to just have a little -- what I would do is I would take Table D and, you know, break it into two parts.

And, you know, it's just -- you know how we're sort of winnowing to make it very explicit? I'd like to see a table with the 25 that aren't in the 11 with just, you know, if it's in Table 1, you have, like, endpoint of most concern and major reasons why chosen, which I think is very helpful, and I think it would be useful for the 25 to just have a table and say why didn't this make it into the top 11? Just a sentence or two.

CHAIRMAN FROINES: Well, I think it could be even easier than that in some ways. I think that part of the problem comes -- I bet you when you contracted these out, you got these literature reviews back, and they weren't sufficiently focused on the issues. You had broad -- you got broad reviews back when, in fact, what we're asking is a very precise question. Is there evidence for differential susceptibility? That's the question.

And so the question -- you could do it with -- almost with a table, which is, is there evidence for

differential susceptibility for the 35? Yes or no. Is there -- is there evidence lacking? Yes or no. Which goes to the question of chemicals are innocent until proven guilty. What is -- what are five references where the answer to one of those -- the first question is yes, what are the five references that would document that answer? And that's it. You've done it.

DR. GLANTZ: Yeah. That would be fine, too.

CHAIRMAN FROINES: It actually is a very straightforward task, if you have a focused agenda. If you want to review the toxicity of arsenic and it's -- and you get a document that's full of all this stuff that has no relevance whatsoever to the question at hand, then, in fact, it's going to become more difficult to wade through.

So my sense is that the question about the 35 is not so difficult if a very focused criteria is established and then answered accordingly with references and with primary references, not secondary reference.

DR. GLANTZ: Yeah. I mean, that would be acceptable to me, too. But, again, I think you just want to make it very -- and, see, then that way people could look at it and say, "Okay. I understand why you drew this conclusion and why you narrowed it down to the

11." I mean, I agree with you.

Ultimately, you're getting to five, but I think at each step of the way, the rationale needs to be very clear. I mean, I don't think anybody here today has said that any -- that the basic approach you've taken is not really reasonable. I think it's quite reasonable.

But for the document to stand, all of this needs to be spelled out in sufficient detail for people to just understand exactly, you know, what you did. And if people want to come in and argue, then they can argue about specific issues, you know, rather than feeling like they're shooting in the dark.

CHAIRMAN FROINES: I can give you a very good example of this I think, and, that is -- I think Paul would agree -- that it's not clear to me why hexane is not on the list. Hexane is a compound with very high exposures, and it's certainly a powerful neurotoxin. And, as Paul said, one can make an argument as neurotoxicity as being equally an important defining feature as asthma is, given the developmental issues in post-utero periods of time or in utero.

So that it's not -- it's not obvious to me why formaldehyde is on the list and hexane isn't. It's not exposure. It's not the level of evidence. So somebody made a decision that is clearly not transparent.

DR. BLANC: Well, let me give you another example. So that, I mean -- something that I can't see here, so I need to see where it fell out. Let's take something that's in the 35, which is methylene chloride. Methylene chloride is metabolized to carbon monoxide. It's one of its main toxicity issues.

Neonatals have -- neonates have a higher concentration of fetal hemoglobin, which binds carbon monoxide much more avidly than other kinds of hemoglobin, which is why in-utero exposure to carbon monoxide, for example, is more of a problem for the fetus than for the mother.

Wouldn't -- and there's a fair amount of sources of exposure to methylene chloride, so there's something where you have clear -- now, you may not -- you're out source reviewer may not have found a study with neonatal pups exposed to methylene chloride, but I don't need that study because I already that it's metabolized to carbon monoxide, and I know from other studies that carbon monoxide differentially affects neonates.

Is that a level of review that happened secondarily in OEHHA that you're confident that things didn't fall through the cracks?

DR. MARTY: We did take those types of

considerations into account. But say for your example of methylene chloride, the exposures in ambient aren't going to produce much carbon monoxide.

DR. BLANC: No. But you're supposed to take into account criteria air pollutants plus exposure to these things.

DR. MARTY: Right.

DR. BLANC: So it wouldn't take much methylene chloride, would it, added to the ambient levels of carbon monoxide potentially?

DR. MARTY: Well, you'd have to do a kinetic analysis, knowing exposures and the rate of carbon monoxide formation and how much that adds to the carboxy hemoglobin load.

DR. BLANC: And I'd have to see your appendix where you said that we did that and --

DR. MARTY: We didn't do that. How could we do that in the time that we had?

DR. BLANC: Well, then maybe it should be 12 because you say we have good reason to suspect that it should make it onto the radar screen. Or maybe there should be 36, and you should never have tried to do the Tier 2.

You should just -- I mean if you can't sit here and tell me that you have such a lack of data and yet

scientific rationale for A, B, C and D but you know -- you know, it goes back to the old saga of I dropped my keys over there but I'm looking over here because this is where the light is on.

DR. MARTY: Okay. Let's back up for a second. Just comment one, Tier 2 does not mean that's the next five in line. That's not what that means. Okay? It means that those rose to the top based primarily on toxicity information. We were concerned about them, but they didn't make the top five. Now, some switching can go on because there was good reason that they actually got to the top 11.

In terms of the rest of the chemicals that didn't make it on, we really -- for this go around, for the first set of listing, wanted strong, toxicology data or epidemiology data to get them on the list. We're going to be looking at all of the TACs under this statute. So the list will be updated over time, but we felt compelled for the first go around to really have strong information.

We can make cases for a lot of chemicals based on just the kind of analogy that you just did for methylene chloride. But where you compare methylene chloride to lead, the weight of the evidence for lead is huge.

DR. BLANC: I'm comparing methylene chloride to formaldehyde, quite frankly.

DR. MARTY: Okay. Well, even if you compare -- at least for formaldehyde, we actually had studies that looked in kids.

DR. BLANC: You had one study of peak flow in kids and a community study where it was one of a variety of things. You know variety and chamber studies of formaldehyde which don't particularly suggest that asthmatics are more sensitive to formaldehyde than anybody else, so --

DR. MARTY: We do have evidence that formaldehyde at low levels impacts lung function in kids. In only one study did they compare adults and children, and in that study, the authors concluded, based on their data, that the adults in the same households were less affected. It's a complicated study. There's no doubt about it. But there we actually we had a piece of information --

CHAIRMAN FROINES: It's not a complicated study. It's actually a simple study.

DR. MARTY: I should not have said that. But my point is that we had information there for formaldehyde. I don't have an equivalent set of studies for methylene chloride. This is not to say we're never

going to look at methylene chloride.

DR. BLANC: But you don't need --

DR. MARTY: It's --

DR. BLANC: But you don't need the same studies because the biological issues are so different. I mean, I'm not harping on methylene chloride per se, but I'm trying to use it as one example. There are so few examples where there is absolutely clear cut biological reasons why an infant would have more toxicologic susceptibility than an adult aside from all of these sort of very generic issues that we're dealing with.

DR. MARTY: It's -- you know, I can't not agree with you. This is a real struggle because you can build cases -- similar cases for other chemicals.

CHAIRMAN FROINES: Part of the question is how does -- for example, we just gave two examples which I think are reasonable, hexane and methylene chloride. How do they end up not on the Tier 2, and non-planar PCBs do occur, and there's -- and the level of exposure of non-planar PCBs at this point in history is vanishingly small.

So here you have hexane, which is in gasoline and a whole bunch of other things, and so you have relatively significant concentrations, the atmospheric chemistry notwithstanding, and you clearly have evidence

of powerful neurotoxicity. How does a non-planar PCB get on this list and hexane doesn't? I don't get it.

DR. MARTY: Again, it would be based on studies in the literature that looked at impacts in either young animals or children. In the case of PCBs, it's both, young animals and children. But we don't have those equivalent studies for hexane at least that popped up during the focus literature review. I don't feel that --

DR. GLANTZ: I guess -- go ahead.

DR. BYUS: I have one question that harkens back to the generic differences between children and adults. How much of that has taken into consideration the uncertainty factors when we do the original calculations, say, for the RELs and the cancer potency? I mean, aren't the uncertainty factors supposed to consider those differences, and then how does that fit in?

DR. MARTY: That's the reason, yes, that we used that.

DR. BYUS: But it should say that in here. It's like we're not ignoring all those things when we do risk assessments for the differences between children and adults. The uncertainty factors are supposed to take that -- some of these things into consideration.

Am I wrong?

DR. MARTY: No. That's correct. Particularly, the tenfold inter-individual variability factor.

DR. BYUS: Right.

DR. MARTY: We have actually a whole other project going to look at whether that tenfold is adequate for some sets of chemicals. But you're right, and I don't think we mentioned that.

DR. BYUS: You didn't.

CHAIRMAN FROINES: Stan.

DR. BYUS: You should mention that because it's important because even though you might not have used these differences between children and adults in construction of this list, those things are, in fact, considered when you do the normal risk assessments with the uncertainty factors.

DR. ALEXEEFF: Let me just --

CHAIRMAN FROINES: Stan.

DR. GLANTZ: I'll wait one second.

DR. ALEXEEFF: I just have a comment in regards to Dr. Blanc's comment. As Melanie indicated, we're not going to ignore the rest of the substances on this list, the rest of the TACs. This is sort of step one of the process. We're expecting that in a couple years to basically come back with all the other ones evaluated.

But before we can do that, before we can do that, we have to develop the criteria. You know, what are the issues? For example, the metabolism issues and stuff like that. We tried in the beginning here to pick the more straightforward ones of which there were data.

In fact, when this whole bill was being discussed, we were reticent to preparing any list prior to developing all of the criteria, but the law was passed with the requirement for a list before we could actually develop all the reasons for why something should be on the list. I mean, it just takes time to lay it out and come up with all the different mechanisms.

So we tried to pick those that we thought were the most straightforward, and so I think part of this dialogue is helpful because it will tell us which types of mechanisms we need to go back and look at to lay out and develop the guidelines or come back with the revised list, not in the next couple months or month, whatever the time line is, but I'm talking about the -- in the year's time frame. That's actually in the statute as well.

But -- so I think hopefully the table that we prepare will clarify some of these issues as to why it didn't make it to the top 11. And that's to say it

wouldn't be something we can't disagree about or have different opinions, but at least it will be clear as to why it didn't make it, and hopefully we can clarify that.

CHAIRMAN FROINES: I think it's important to say that we understand that you operate under a tight time frame and were basically doing the best you could under the circumstances given that we have a July 1st deadline for the first five. So I don't think anybody at this table is not appreciative of the short time frame that you're operating in and the level of effort that's required.

And the tension comes because this is such an important process that everybody's trying to do it right. And clearly it's going to get much better as we go down the road when you have a time to develop these documents in a more thorough and careful way.

And so what's happening is that people are critical of the -- of what was produced. I think that goes without saying. And -- but it's intended to set the process right so that we have everything as clearly defined as possible as we move down the road so that this panel can do its job adequately and that people who represent the public and various interests can understand what's going on.

So I think the context is a supportive one, but it's also a critical one, and we're going to be very critical for the rest of the day. And -- but, again, it's within that context, so nobody needs to feel as though we don't understand that this wasn't a difficult exercise.

But I do think that it's really important that we do better on defining criteria and the basis for decision making, which is what's been said a number of times.

DR. GLANTZ: I'd like to come back to the list. I understand what you're saying, George and Melanie, you know, that Tier 2 doesn't necessarily mean that that's the next five. But as a practical matter, I think if you read the public comments and the people in the audience, you know, the people who make acrolein would rather not see it on the list at all, you know -- or I just picked that out because it was the top one.

And I think the question -- I mean, I have some concerns about which is in Tier 1 and Tier 2 of those 11, but I think before we get to that, I think it would be worth asking the panel: Is there anything that's in Tier 1 or Tier -- and we don't -- it doesn't have to be 11, but I'd rather it wasn't 35, you know? I think we want to table the report to be the ones that are deemed

the most important, and, you know, maybe some new information will become available over the next year or two that will make you want to change that.

But I think the question is: Is there anything people think is in Table 1 in the report, the ones that they've picked as the top 11, that doesn't belong there in the top 11 or 12 or whatever we thought was reasonable? And is there anything that's been in Table D that isn't in the report that ought to be, without throwing the whole list in?

I think, you know, the prioritization process is an important one, so I think trying to keep these lists about how long they are is a good idea. But several things have been kicked around. They're not things that I personally know a lot about, so I just ask the panel: Is there anything on Table D that isn't in Table 1 in the report that we think ought to be looked at? That it ought to be.

And, conversely, is there anything -- I've heard some comments about formaldehyde, for example, and seem to suggest maybe it shouldn't be given a priority. So I'd be interested in any comments. You people know more than I do.

CHAIRMAN FROINES: I think Paul's point, though, is well taken insofar as that question, in a

sense, presupposes that we've had a chance to look at some of the reviews in the literature.

DR. GLANTZ: Yeah. But there's going to be -- there's going to be another draft of this. But I think in order to give OEHHA some guidance, is there anything that people think, you know, ought to really be seriously --

CHAIRMAN FROINES: To answer your own question, do you?

DR. GLANTZ: I don't. I would move some things around on the list of the report. I don't. I mean, does anybody else?

CHAIRMAN FROINES: Craig?

DR. BYUS: Uh-uh.

CHAIRMAN FROINES: Roger?

DR. BLANC: Well, I do. And I'm going to put it in a slightly toned down version. I have things for which I would be so concerned that it would be -- I would be going through a -- an appendixed thing, and I would be getting on Medline and making sure that something hadn't been missed. So let me tell you each of those and why, and some of them I've already mentioned.

I would be extremely concerned about carbon disulfide because of its cardiovascular effects and

because of its central nervous system toxicity and because I know that it's out there as an important ambient.

I would be concerned about chlorine because it's -- other than sulfa dioxide, it's the only other chemical for which there's good evidence that person's with airway hyperactivity have a more extreme response, and; therefore, if there's any chemical on the list for which asthma ipso facto is going to be something that you're going to then say "Children must be doing worse," chlorine would be one of the chemicals. And, in fact, the REL for chlorine is based on the response of people with airway hyper-responsiveness.

I would be extremely concerned about manganese, even if levels in the atmosphere currently are trace because we have an extremely important reason to --

DR. BYUS: Paul, go back to the last thing you said about chlorine. If that's what the REL is based on, then would you need the extra considerations for it?

DR. BLANC: According to this, yes. I mean, as I read the statute --

DR. BYUS: Okay.

DR. BLANC: -- it doesn't even matter.

DR. BYUS: I'm sorry.

DR. BLANC: No, no. Methylene chloride for the

reasons that I've said in terms of carboxy hemoglobin and in terms of the statute's requirement to consider interactions for priority air pollutants.

And those are the ones I believe that I would want to look at more closely.

DR. GLANTZ: Is there anything on -- in Table 1 in the report that you think probably shouldn't be there compared to these other things?

DR. BLANC: I actually don't want to -- I'm not prepared at this point to discuss it from that.

DR. GLANTZ: Okay.

DR. BLANC: Because I think the -- I'm taking -- we have enough data to review whether or not they felt that there was enough to rise up, at least into some group that needs to be considered as a candidate for the five.

I'm really addressing a much different question which is -- and I take what you say at face value that because something isn't among the 11, it doesn't mean that it won't get looked at closely, but let's be realistic. It's going to be a harder sell a year from now to then suddenly move something up from being off the radar screen to being something -- I mean, I'm just looking at it from sort of a public health point of view. So I think this is not a trivial question

necessarily.

DR. ATKINSON: But then that does point out the need to -- I think you need to put some more verbiage about the ambient concentration data. I mean, you just say that you take it from ARB's database. I think a little more discussion of what that database includes, the air basins it was taken in and so on and some caveats that, you know, it's not -- may not be -- may not really be correct, and there may be interferences, and there may be and are data from other studies which may really supersede those.

DR. BLANC: I guess one technical question, Melanie. Methyl bromide, which is No. 23, but is -- it is a fumigant, but it has other uses, and that's why it was allowed to stay here because everything else --

DR. ATKINSON: It's a pesticide.

DR. BLANC: Everything else has fallen off.

DR. ALEXEEFF: That's right. Methyl bromide is on the list because there is the Hot Spots Law which requires permitting of stationary sources of which fumigations chambers are stationary sources.

DR. BLANC: So ARB does --

DR. ALEXEEFF: That's why that one --

DR. BLANC: So ARB does --

DR. ALEXEEFF: Well, the air districts do that,

yeah. So that's why that is on that list.

DR. BLANC: Well, then that's probably another one I would say I would be very suspicious about of the list.

And, John, maybe you have some others, particularly some of the other heavy metals that I haven't talked about.

CHAIRMAN FROINES: Gary?

DR. FRIEDMAN: No, I can't add anything.

CHAIRMAN FROINES: I want to avoid getting into giving you a long list because I think it would be useful to give you a long -- to expand the list of 11 to a larger number, perhaps not 35, but a larger number, but I don't -- I don't know.

Acetaldehyde fits into your generic issue of small airways irritants, so it's obviously one for which it could be on the list. In that sense, if you have an expanded list, it probably should be on the list. But then you have a problem with glutaraldehyde, for example, and crotin aldehyde. The aldehydes, given the criteria of small airways and irritant effects, as we know, there's a whole list of aldehydes that would fit that criteria. But acetaldehyde would be one.

And then obviously the metals, arsenic, cadmium and chromium are a second group of three, and obviously

I even pointed out hexane. But I'd rather sort of not give you that as a list. I'd rather give you that as a list based on looking to see if there's evidence of differential effects. Do you see what I'm saying?

In other words, I think that I would expand the list. Paul was actually making some decisions, for example, with methylene chloride that he says that there is evidence of a differential effect. And so, therefore, that could reasonably be on a list without necessarily going through all the toxico-kinetics and metabolism issues that one might have to look at.

So I can give -- I can mention those compounds, but I would rather look at the reviews and see to what degree you think butadiene, for example, which is a very important compound, has any evidence of differential toxicity. And if it does, then I would put it on the list. Do you see what I'm saying?

DR. ALEXEEFF: Well, I think --

DR. BLANC: Assuming that they did that and there wasn't, I guess?

CHAIRMAN FROINES: I don't know that. No. Because I don't agree with that. You assumed that and there wasn't, but that's wrong when you consider hexane because hexane there is evidence of differential effects to the degree that you think of neurotoxicity as having

some generic elements to it.

DR. MARTY: I think just a couple comments. I am not trying to be argumentative.

CHAIRMAN FROINES: That's okay. I understand that all the generation may not necessarily have a developmental characteristic. And so the mechanism of CPDA does not necessarily give you evidence for a developmental effect. I understand that with hexane, but it's still -- the neurotoxicty question is still one that needs to be evaluated.

DR. MARTY: All right. I agree. We debated endlessly whether, for example, all neurotoxins should be on the list because there's lots of reasons to think a developing organism would be more sensitive to them.

Data -- genotoxic carcinogens, there's a lot of mitosis going on. You would anticipate a larger number of targets for mutation so forth and so on. And we did have a lot of concern about chlorine, but when we looked at chlorine concentrations in the air compared to the reference exposure level against acrolein concentrations in the air compared to the reference exposure level, acrolein wins out.

DR. BLANC: I'm not making argument for acrolein not to be on the list, am I?

DR. MARTY: No.

CHAIRMAN FROINES: We're also not clear why your list has 11 chemicals on it. That's the question that's being raised.

DR. ALEXEEFF: I think there's --

DR. BLANC: Before you answer that, George, I just want to say that what is very confusing about your last statement, Melanie, is that the way you explained it is everything made it to D already because of importance in its ambient levels to REL or its inherent toxicity. And then the thing that makes something jump from List D to the final 11 is levels of evidence of a differential effect in kids.

And your answer about chlorine was, yes, there is evidence that it would differentially affect asthmatics and, therefore, the kids in our rationale, but the concentration levels weren't that high in the air. But --

DR. MARTY: It was also extent of exposure. Within the list of 35 or 36, Stan, we also had concerns about extent of exposure.

DR. BLANC: That would have kept something from getting to the top 11, even though that's not what you said previously?

DR. MARTY: Actually, it's on the slide.

CHAIRMAN FROINES: Yeah. But that doesn't -- I

mean, but how do you get with non-coplanar PCBs?

DR. MARTY: That's weighting heavily the toxicity. Also PCBs are virtually everywhere in every body.

CHAIRMAN FROINES: That doesn't mean a thing. And in terms of -- I mean the notion of is there a potential for exposure that somebody can then go do something about as a public health issue is what this is all about. This isn't about making decisions strictly on the basis of toxicology. The idea is to protect children and because -- and the way you protect children is through various control mechanisms.

So if you have something that can be controlled, then that's a consideration that goes into the risk management phase, and I understand all that rhetoric. But I still think it's the underlying consideration. The underlying consideration of the law is to protect children.

Therefore, if you have something that for which the exposure may be very widespread but doesn't occur through an ambient or airborne pathway, because we're focused on air issues now, and resulting in a contamination of soil, water or what have you, then we have to be careful to put that as a high priority it seems to me because it's not clear we can do anything

about it.

DR. MARTY: That's actually why it ended up in Tier 2 instead of Tier 1. And Tier 2 just means those 11 that didn't end up in Tier 1, there's no other significance to Tier 2. I agree with you. You know, there was a case where we had strong epi and tox data, but we felt strong enough to say, "There's differential impacts here," but then when you go to look at the exposure piece, you know there's exposure, but is air an issue?

We think it's an issue for dioxins, but it may not be the -- certainly it's not the driving pathway by which you're exposed to PCBs.

DR. ALEXEEFF: I just wanted --

DR. GLANTZ: There's nothing, you know -- I just want to reiterate, while the law says you have to pick five, the law doesn't say you have to pick 11 for this -- you know, and have your Tier 2. So it may be that you might want Tier 2 instead of having six things in it to have eight or nine.

I don't think -- I personally think because of -- for the reason somebody made that once this is done, it's going to be hard for things to jump into that list. I mean, I don't think you want to put all 35 or 36 of these things in. I think you've gone through a

fairly rational winnowing process, but I think Paul mentioned three or four more that ought to be seriously looked at, and it may be that in the final report instead of 11, there's 15, you know? Plus what everybody else says.

DR. ALEXEEFF: There's -- you know, in terms of reaching the group of 35, a lot of the general type of issues were on the minds of the staff in terms of putting them there, such as the issue of methylene chloride in terms of metabolism in carbon monoxide. That actually was certainly discussed. And the manganese and a lot of those chemicals were put in the top 35 because of knowledge of the general type of issues.

And then -- and so I think once we put that on the table, that could help clarify as to why it made the top 35.

DR. GLANTZ: Yeah.

DR. ALEXEEFF: And then the next question is, well, how come it made -- it did or did not make it to the 11? And I think that what we could do for the ones that you -- we've counted seven, six or seven. We could provide additional summaries. Seven compounds have been mentioned here.

CHAIRMAN FROINES: More if you take mine.

DR. ALEXEEFF: I wasn't taking -- you said you weren't really proposing all of yours, but let me just finish my sentence.

CHAIRMAN FROINES: But it's a rhetorical statement; right? It says "arsenic." I want to know whether or not your summary has evidence for differential effects, and if there's evidence, then put it on.

DR. ALEXEEFF: Yeah. We'll put that in the -- you'll see it in the generic type of table; okay? And explain why it drops out. But we could do is provide summaries for a number of additional ones for which there is some evidence on that. The question comes with something like if -- and I can't remember methylene chloride, but if it's more of a mechanistic inference, but there isn't really actually any studies we can come up with -- although, it's, you know --

DR. BLANC: Well, I would say that that would be an example for something where the logic is so concrete that you don't actually need the specific study.

DR. ALEXEEFF: Yeah. Well, that's kind of the question.

DR. BLANC: If A equals B and B equals C then A equals C. So if you have studies that show that it is

metabolized to carbon monoxide, which you do, and if you have other studies of carbon monoxide which show that there's a differential effect in children, which you do, then I don't think you need the study of methylene chloride in children.

DR. ALEXEEFF: Right. Anyway, we can prepare summaries for a number of those compounds and then the panel can decide whether they're relative to --

CHAIRMAN FROINES: When you add in carbon monoxide.

DR. BLANC: Yeah. And there has to be some comment on -- you know, some REL-type argument about, you know, potential for exposure to carbon monoxide as a particulate air pollutant.

DR. ALEXEEFF: We've done carbon monoxide under the other part of this particular statute. We just completed a complete review of carbon monoxide.

DR. BLANC: And then, for example, for manganese, which of all of these I guess I would make the argument that is the one where you have the most chance to have a real public health impact from this document. And if the whole reason why -- I mean, I want to look very closely that you have absolutely no -- you know, data, other than inferential data, of any susceptibility of young animals to manganese. Because

if what kept manganese off this list does not have enough current air pollution data for manganese, then I would say -- I put it No. 1 of the 5 because that's the one you don't want to have the air pollution for.

DR. ALEXEEFF: Actually, there is ambient data on manganese. It's on the table.

DR. GLANTZ: But the point Paul is making is he's concerned that there's going to be a lot more.

CHAIRMAN FROINES: It's an additive issue.

DR. MARTY: You know what? I thought we had -- Kirk, is there not a statute banning the use of the organo-manganese compounds in gasoline in California?

MR. COLLINS: Yes. In 1977. We've got copies of it because this came up a couple years ago. There is a statute banning the use of it.

DR. BLANC: The EPA hasn't banned it yet.

MR. COLLINS: Correct.

DR. MARTY: That's right.

DR. ALEXEEFF: But California has.

DR. MARTY: And that -- you know, we have the same, identical concerns about manganese. That compound makes me nervous, and I think it's nuts, personally, to put it in gasoline.

DR. ALEXEEFF: But what we could do is we could research that issue, and if that's our reason for not

putting it on the list, that it's not going to be used in gasoline, we could lay that out, you know, the statute, cite that, and we can clarify that issue.

DR. BLANC: And were that statute ever to be reversed it would --

DR. ALEXEEFF: That would be what the information is.

DR. FUCALORO: You're talking about -- excuse me. I'm sorry I'm late.

DR. BLANC: We're talking about this list --

DR. FUCALORO: Manganese.

DR. BLANC: -- here and why things that are on this list aren't among the -- that only 11 of these --

DR. GLANTZ: Does Gary have anything to add?

DR. FRIEDMAN: No, I have no other comment.

CHAIRMAN FROINES: Melanie, tell me -- why don't you -- I don't think we can get to your asthma slides before lunch, so why don't you finish this phase.

DR. GLANTZ: Are we going to talk about Tier 1 versus Tier 2 before lunch?

CHAIRMAN FROINES: No. It's almost 1:00 o'clock.

DR. MARTY: I think we should go chemical by chemical --

DR. GLANTZ: Okay.

DR. MARTY: -- to do that.

This slide is just what you already know, in alphabetical order, the proposed listing, which is equivalent to Tier 1 as described in the document. And then, Andy, the next slide just shows those that fell out and didn't make it to Tier 1. And then I have asthma slides which I --

CHAIRMAN FROINES: We can come back to the asthma slides, but I think Stan would like to talk about Tier 1 versus Tier 2, but my assumption is that that would be best done as we go through the level of evidence on the individual compounds, but if he wants to --

DR. GLANTZ: Whatever.

CHAIRMAN FROINES: -- argue it differently, that's fine.

DR. GLANTZ: Just so we get to it. Whatever you want.

CHAIRMAN FROINES: Well, it's whatever the panel really wants.

DR. FRIEDMAN: I think it would be helpful to just -- if it's not a long topic to deal with that before lunch.

DR. GLANTZ: I think that diesel exhaust should be in Tier 1. It's a fairly brief comment. The -- I

mean, when you read the report, you know, there's a lot of, kind of, perseverating about why it isn't in Tier 1, and I think that it belongs there. I think it's very potent.

Several of the other things that are in Tier 1 are in diesel exhaust and I think that evidence it's important and all the things we've been talking about are very strong, and I think since we can only have five, I would suggest that benzene be dropped down to Tier 2.

Because I think in reading -- again, reading the document and reading the public comments, I think the -- that's -- of the things that you have there, some of you guys know more about some of these other compounds than I do or chemicals than I do, but that's the one that I think if you had to pick one of those to move down, that's the one I would suggest moving down.

CHAIRMAN FROINES: Elinor, you know, did her thesis with Martin Smith at Berkeley, and she worked on benzene, so she was strongly opposed to the benzene thing.

DR. GLANTZ: Well, we normally have five. I'm not saying we should all go out and drink benzene for lunch.

CHAIRMAN FROINES: I was just joking.

DR. GLANTZ: Okay.

CHAIRMAN FROINES: I think you opened such a pandora's box. That's why I would want to do it after lunch when we actually have -- I meant it as data.

DR. FRIEDMAN: Yeah. I thought we were just going to talk about criteria, not about specifics. That's why I didn't understand.

DR. GLANTZ: Well, he asked me about the specifics.

DR. FRIEDMAN: That's why I --

DR. BLANC: Well, we have a foretaste of what we'll be discussing after lunch.

CHAIRMAN FROINES: Why don't we take lunch and then have the asthma discussion. And then as one of the criteria, which I think is what Melanie was planning as an important criteria, and then go to the individual chemicals. Does that make sense?

DR. GLANTZ: Where do we get lunch, and what time do we need to be back?

CHAIRMAN FROINES: I don't know. Jim or Peter?

DR. BLANC: Downstairs in the cafeteria.

CHAIRMAN FROINES: Downstairs in the cafeteria.

DR. FRIEDMAN: John, may I request that we have a rather short lunch because I have to leave at 3:00 o'clock, and I'd like to hear as much as possible.

CHAIRMAN FROINES: Half hour? Forty-five minutes?

DR. BLANC: Thirty-five minutes.

DR. GLANTZ: We've got to find the place.

CHAIRMAN FROINES: Thirty-five. And we are going to start at 1:35, so let's -- the panel should -- the audience doesn't necessarily have to do that, but the panel members do.

(Luncheon recess.)

CHAIRMAN FROINES: Before we start, Dr. Fucaloro would like to make a comment to the panel.

DR. FUCALORO: Yeah. I have to report an ex parte contact with a gentleman who actually teaches a course at our college in environmental law. He is an environmental lawyer, and he's working for people who reported in these contacts on the issue of lead.

So, basically, we discussed some of the issues concerning inclusion on that list of five. And he, of course, wants lead out. "Get the lead out," he told me. But, of course, let the science do the talking. And we just discussed it. I think his basic argument was what was made in this report, which essentially states that the toxicity of lead is high. Its -- the exposure level is low. That's about it.

CHAIRMAN FROINES: Kirk, is there anything more

we need on this issue besides having it on the record?

MR. OLIVER: No.

CHAIRMAN FROINES: Well, that was the most succinct exchange we've ever had.

DR. GLANTZ: Well, then I need to comment.

CHAIRMAN FROINES: This is where you would want to fill it up.

DR. GLANTZ: Just joking.

Melanie is fortified and ready for another round.

DR. MARTY: Are we ready?

CHAIRMAN FROINES: She's in danger of developing pugillus encephalopathy by the end of the day.

DR. GLANTZ: What is that?

DR. BLANC: Getting hit on the head too many times.

DR. MARTY: It's the Mohammad Ali syndrome.

I'd like to start this afternoon by talking a little bit about asthma because we use asthma -- exacerbation of asthma as a toxicological endpoint in some of our arguments for differential susceptibility of children versus adults. I just wanted to flesh that argument out a little bit.

The asthma prevalence rates in children are

higher than adults. There's reasonably good statistics on that from the asthma surveillance program at CDC. So as on a population-wide basis, other things being equal, if you exacerbate asthma in a population, you have more kids likely being impacted than adults.

Also children have smaller airways. This came up earlier in the discussion. So constriction of the airway, which happens in asthma, will cause a greatly increased resistance. The resistance is inversely proportionate to the cube of the radius. So as you -- it's not a linear increase in resistance. It's quite a bit more than linear.

So when you have a child with a small airway, and they have an asthma attack in that the mucous secretion blocks the airway as well as the broncho-constriction, they can quickly get to the point where the increase in resistance to air flow causes a very severe problem in a child and less so in an adult who is starting out with a larger airway.

I'd like to add also that hospitalization rate data indicate that it's highest for the zero to four-year-old age group, and I'll get to that in a minute. And also asthma prevalence --

DR. GLANTZ: You mean hospitalization rates for asthma?

DR. MARTY: Yes. Right.

DR. GLANTZ: Not hospitals --

DR. MARTY: It's actually based on discharge data so -- and what the discharge data indicates what the person is in the hospital for.

DR. FRIEDMAN: Are you saying that they're highest among other -- taking zero to four year olds' asthma rates are the highest cause of hospitalization, or are you saying that given you have asthma, you're more apt to be hospitalized if you're zero to four?

DR. MARTY: It's if you compare by age groupings zero to four, five -- I forget what the age groupings are. But the highest rates, according to the discharge data are for zero to four year olds, and it drops out as you get older.

DR. GLANTZ: But the question here is what's the denominator?

DR. BLANC: Per 100,000 children.

DR. GLANTZ: No, no. Is this --

DR. MARTY: You know what? I have a slide on that, so maybe we should talk about it when I get to the slide.

DR. GLANTZ: Okay.

DR. MARTY: The asthma -- I just wanted to add in that the asthma prevalence, at least in the U.S. and

elsewhere, is increasing. There have been large increases over the last couple of decades. So it's an important disease.

Next slide, Andy.

DR. FRIEDMAN: Wait. I have to -- can I interrupt? I always want to acknowledge Stan's help in asking my questions. Thank you, Stan.

DR. MARTY: Some of the discharge data, you can get either on a national basis from the CDC, or the Department of Health Services puts together a report, asthma hospitalizations by county, and they break it out by age and sex and race.

And if you look at overall hospitalization rates, it's 216 per 100,000 discharges. So, in other words -- right. The hospitalization rates for children are much greater than for adults. The rates for kids under one year old are three times that of the rates of 10 to 14 year olds, which goes hand in hand with the smaller airway phenomenon.

Next, Andy.

DR. BLANC: Just say that the rate for hospitalization is higher among children. I don't think you can connect the dots and say it's because they have smaller airways. Just -- you're certainly on firm ground if you say that children -- per 100,000 children

have higher hospitalization rates in that age group than in older age groups and leave aside the issue of the airways with that.

DR. MARTY: Okay.

DR. GLANTZ: I still don't understand per 100,000. Is it per 100,000 children?

DR. MARTY: Discharges.

DR. BLANC: No, no. Per 100,000 children.

DR. MARTY: Mark is telling me it's per 100,000 kids.

DR. FUCALORO: In that age group, so that it's standardized within the age group.

DR. MARTY: Yes.

DR. GLANTZ: So it's not per 100,000 hospital discharges. It's per 100,000 --

DR. MARTY: No. It's per 100,000 kids.

DR. BLANC: For 100,000 children, the rate of hospitalization is higher than per 100,000 adults.

DR. GLANTZ: Yeah.

DR. MARTY: And I did want to point out that hospitalization, that's not doctor visits. That's not going to the -- it's the doctor telling -- the doctor is the person who puts you in the hospital. It's not you going to the hospital saying, "I need to be hospitalized." So I think it's a little more firmer

ground for looking at a differential effect between kids and adults than just going to the doctor.

CHAIRMAN FROINES: I -- Melanie knows I'm going to say this because she knows how I feel about it. I think that the behavioral factors associated with going to hospitals is so complicated that I think this is such a poor example.

I mean, more -- you look at asthma rates, more whites go to hospitals than blacks go to hospitals, but that doesn't argue for a differential susceptibility of whites over blacks. It has to do with socioeconomic status.

DR. BLANC: I don't --

DR. MARTY: Can --

DR. BLANC: John, listen. I think you're beating a dead horse. There's no -- no one doubts that the rates of asthma among children, the prevalence. The incidents of severity is higher among children than it is among adults. Certainly until you get up to the very old age of adults, and then it goes up again. So it will be a question if you were talking about 75 year olds.

But since your task is to say, you know, is this a disease for which the rates are higher among children, especially young children, that's not an

argument. That's not -- there are, of course, many other diseases which are also at very high rates among children compared to adults, but that's not the point of this discussion either.

DR. MARTY: Right. Okay. Andy, next slide. This is just a figure taken from this document of Age-Adjusted Asthma Hospital Discharge Rates For Kids Ages 0 to 14 by Race and Sex. And, actually, African-American kids have very high rates of hospitalization for asthma relative to other race groupings. And that's discharges per 100,000 kids and boys for some reason more than girls.

DR. BLANC: And then it changes again but yes.

DR. MARTY: Next slide, Andy.

And this was just a different look at the data by age group across a couple of years, and this is California-specific data. Again, discharges per 100,000 by age. So the top line is less than 1, then 1 to 4, then 5 to 9, then 10 to 14.

So this is the -- this is more data looking at office visits per thousand by age group, for asthma. ER visits per thousand by age group for asthma and hospitalizations per 10,000 by age group. The groups are big here: 0 to 4, 5 to 14, 15 to 34 and so on. So I think that --

CHAIRMAN FROINES: I think I'm afraid I still feel that Paul's right, that this is not an argument for differential susceptibility to chemicals.

DR. FRIEDMAN: It is an argument for differential impact, you know, on this group in terms of the costs of their care and days lost from normal activities. Is that part of the consideration?

DR. MARTY: Yes. Right. That's all we had for -- in terms of introduction. We have a presentation on each one of those 11 chemicals. We can start with --

CHAIRMAN FROINES: What's the -- what's the conclusion -- having given that presentation on asthma, what is the conclusion that you draw as a basis of your criteria for defining susceptibility? What's the bottom line from all that?

DR. MARTY: Well, the bottom line is that OEHHA takes the position that things that exacerbate asthma are going to have larger impacts in children on a population-wide basis than on adults.

CHAIRMAN FROINES: Okay. Exacerbate asthma, that's one criteria. That's different than evidence of a chemical having irritant effect.

DR. MARTY: Yes.

DR. BLANC: Well, a generic irritant wouldn't necessarily exacerbate asthma.

DR. MARTY: I think that the data show that there are some irritants that don't necessarily exacerbate asthma or that you can't see it in the studies.

DR. BLANC: Well --

DR. MARTY: I don't think you could make that argument that every irritant exacerbates asthma.

DR. BLANC: Are you -- well, let me ask the question in a different way. Is what you're -- your threshold then would be evidence that if you compared asthmatics to non-asthmatics at the same exposure level, that consistently the asthmatics would have a greater increase in airway resistance in response to the same concentration of the pollutant in question, and that's what it would be?

DR. MARTY: That may be true, but that's not our argument.

DR. BLANC: Then --

DR. MARTY: Our argument is that --

DR. BLANC: How would you then differentiate -- that's the way that I'm familiar with making the argument that a chemical irritant -- because I think it is a reasonable thing to say that most irritants would tend to create a problem across the board in airways, if they're water soluble particularly.

And, therefore, if you started from a narrow caliber, the implications of having inflammation would be worse if you already had narrowed airways. This would be true generically for every single irritant and would only be a matter of irritant potency.

If you're making the argument that, in fact, a particular irritant would be more prone to induce broncho-spasm in people with preexisting airway hyper responsiveness, as opposed to people without preexisting airway hyper responsiveness, then your list of substances is vanishingly small. And, in fact, it really is sulfa dioxide, sulfa dioxide and sulfa dioxide, which is a criteria air pollutant.

If I had to then say beyond that what -- do I believe that there is experimental evidence that is consistently shown? And I would be very hard pressed. There certainly has not been consistent evidence for ozone, again, I grant you, as a criteria pollutant. There has not been consistent evidence for nitrogen dioxide, and it's been -- or oxides of oxygen, and it's been a big area of controversy.

There certainly is not such experimental data for formaldehyde or other aldehydes. And for chlorine there's -- you know, there's one small study that suggests that -- what a -- I know because I did the

study and am waiting for somebody else to repeat the results. So that's why it's going to be --

DR. MARTY: That's why we're looking for chemical-specific data.

DR. BLANC: -- difficult for me.

DR. MARTY: And it's in -- you know, when we say something is exacerbating asthma, we're using studies that show it exacerbated asthma rather than saying "because it's an irritant, it probably exacerbates asthma." That's where we're drawing a distinction for this set of 12, 11 compounds.

DR. BLANC: And so, therefore, when we come back to the individual studies, that would be the issue that you are raising?

DR. MARTY: Right. Right. It's not that we don't have concerns about some of the other irritants for which there are direct studies, you know. It's not that we're not worried about that. We are worried about that.

DR. BLANC: But if you theoretically had an epidemiologic study that had an association in a mixed exposure and you had laboratory control human exposure data that did not show the effect, wouldn't the laboratory data argue more convincingly that the epidemiologic association in the mixed exposure

situation was -- couldn't be used to single out, perhaps, the substance that made you worry?

DR. MARTY: Well, it's a hypothetical. I'd have to look at the studies. But I think it's also important to remember that we're supposed to consider multiple pollutant exposures. I mean, it's difficult to say in a lot of the pollution epi studies which pollutant is the worst actors. Probably interactions.

DR. BLANC: And then in terms of your rank, hierarchy of conditions and -- for which particular concern would be important among the pediatric population, so hospitalization rates for upper respiratory infection are probably higher among young children than among adults, by and large.

DR. MARTY: I'm recollecting that that's the case.

Mark?

DR. BLANC: So, therefore, if there was an irritant pollutant that was associated with a greater risk of upper respiratory, secondary infection, then that would also be by the same logic something that would be relevant?

DR. MARTY: Yes.

DR. BLANC: And if something, theoretically, was associated with aggravated hyperglycemia, since

hospitalization rates -- were hospitalization rates were to be higher, or juvenile diabetes, which it probably isn't, but opposed to adult onset diabetes, since it's such a big, burden disease. But I'm just saying it's not specific.

There's nothing peculiar about asthma -- for asthma per se. It's just that it's -- one, it's a common disease, and it's a common disease among children, and for children less than four, hospitalization rates are higher. But were there to be other conditions that were in the same category, they would also logically be on the same level on concern.

There's nothing inherently about asthma that has your attention in terms of --

DR. MARTY: It has our attention because we're dealing with airborne pollutants, some of which we know exacerbate asthma.

DR. BLANC: Well, no.

DR. MARTY: I don't know which ones --

DR. BLANC: What are some of them -- what are the some of them that you know exacerbate asthma? You listed formaldehyde. I think your evidence is, you know, convincingly weak, but other than that, what else do you have of evidence?

DR. MARTY: Acrolein, particulate matter,

sulphur dioxide, nitrogen dioxide.

DR. BLANC: Well, sulphur dioxide is not on the list of --

DR. MARTY: Right. Right. But what I'm saying is there are air pollutants out there for which there are good evidence that they're associated with the exacerbations of asthma.

The other hypotheticals about agents that would interfere with glucose metabolism, I don't know if there are chemicals out there that do that that were listed as TACs. So, you know it's --

DR. BLANC: Again, it's theoretical. I'm just trying to get the examples on the table so I can understand all the thinking process. That's all I'm trying to get at.

CHAIRMAN FROINES: Well, I think the other point -- the other point that I'm trying to get to is I think in the end we want a document that lays out the criteria quite explicitly, and here we have a very specific criteria, which is the exacerbation of asthma, and that's associated with small airways and so forth. And you're not including most irritants necessarily in that criteria.

So we just need -- when we finally get a full document that those criteria become very well defined so

that everybody who reads the document knows exactly what the basis of the decision making was.

DR. MARTY: Okay.

DR. BLANC: And, you know, the problem with -- you don't want to over weight asthma because it's easy to diagnose and the hospitalization rates are clear since no one gets hospitalized for having lost five points of their IQ, you know, due to a chronic neuro-toxicant. So, you know, there's that issue also to be contended with.

And I think you're going to need to be very explicit that, you know, using this criterion for this health endpoint doesn't mean that there are other health endpoints, which are probably a great deal more -- well, that could be at least as serious if not more serious.

You allude to those as though they're not there, but you do talk about them.

CHAIRMAN FROINES: Paul, do you want to raise any questions about criteria at this point, or do you want to save it until we go through the chemicals?

DR. BLANC: You mean criteria for how -- generic criteria other than the asthma?

CHAIRMAN FROINES: Yeah.

DR. BLANC: I think we talked about to an extent earlier the issue of things which are -- have

neurotoxicologic mechanisms in general for the CNS and their implications generically for the developing organism, and I think that that's an area in which your criteria also need to be explicit.

It may not require the same degree of -- well, you should spell out what kind of evidence-based criteria you would need or not need because there you're -- the argument is so direct and so biologically obvious that things which are CNS neurotoxins are going to differentially impact the developing nervous system of an infant.

DR. MARTY: We did in the introduction go through several organ systems that we thought were critical.

DR. BLANC: I know. I know. I know. I'm just saying.

DR. MARTY: It's not spelled out enough, though, is what I'm hearing.

DR. BLANC: Well, I think that later on -- because that's buried in a whole generic discussion about theoretical ways in which -- in which children could be at risk but it's not -- it's never translated into, therefore, what kind of information we would be looking for from human studies or from animal studies that would support an effect.

I think that there's another area of the document that's a bit murky in terms of what your thinking was. If you want us exposed to something which is a clear teratogen, and then an infant is born without legs and then has a normal, legless life span, your argument is not that -- or is it, that being legless in childhood has a differential impact on your childhood as compared to your adulthood?

DR. MARTY: The argument would be that if you had that exposure as an adult, you couldn't possibly have that effect. That's the argument.

DR. BLANC: But you're not even a child yet. You're in utero. So why are children -- the law has to do with infants and children, not with fetuses. So at what point -- I'm not trying to make an argument here. I'm certainly not trying to make any kind of, you know, backdoor, you know, discussion about, you know, when life begins, et cetera, but I'm trying to understand your thinking.

And when -- what you consider a child in terms of -- or an infant and what your criteria for considering pre-term exposures are in terms of susceptibility, because there was a subtext in this document which seemed to imply that you considered any pre-term exposure for which there was fetal

susceptibility as being evidence of childhood -- childhood sensitivity.

And did you, in fact, have your legal counsel comment to you on whether or not that was within the scope of the law as written, since the law does not mention fetuses or prenatal exposure?

DR. MARTY: I think it's impossible to argue that developmental toxicity does not impact infants and children differentially.

DR. BLANC: Yeah. But over adults?

DR. MARTY: Because if you get the exposure as an adult, you don't have the developmental toxicity.

DR. BLANC: But they haven't gotten it as a child either. They've gotten it as a fetus.

DR. MARTY: I don't think that maturation of the organ system cares whether it happens in utero or postnatally. If the impacts are because the organ system is maturing, that doesn't occur when you're an adult. Then there's the argument for differential impacts.

I would like to point out that we don't think that all developmental toxins should automatically be on the list because there's exposure consideration and how potent it is as a developmental toxicant.

DR. BLANC: But let's say, theoretically,

thalidomide were an air pollutant. You would say it should be on this list; correct? I'm just trying to understand.

DR. MARTY: If there was exposure and so forth and so on.

DR. BLANC: Yeah. If it was an air pollutant, if there was a toxic air pollutant called --

DR. MARTY: It should be considered.

DR. BLANC: And based on the available evidence, it would -- assuming that there was exposure, it would be --

DR. MARTY: It should be considered for listing.

DR. BLANC: Based on that effect.

DR. MARTY: Right.

DR. BLANC: I'm just trying to understand your -- I think that you need to be even more explicit than you are that in fact an isolated teratogen would be considered because -- for the argument that you just made, if that's the argument you want to make. I'm not sure that that was the intent or not the intent of the legislation, but if that's your interpretation of it, at least you should be explicit about it, even more explicit.

I mean, it is there because it keeps coming up

in your rationale for considering things.

DR. FUCALORO: Just thinking it through, again, I know alcohol is not an air pollutant that we're talking about but a mother using alcohol would then be -- if that were an air pollutant, wouldn't that be -- fall under the same category as thalidomide?

DR. BLANC: By their --

DR. FUCALORO: By their definition.

DR. BLANC: Yeah. I assume so.

DR. FUCALORO: Of course I -- so something that a mother is exposed to that the kid may -- that a newborn may not be exposed to, isn't that where we're going?

CHAIRMAN FROINES: No. That's not the issue.

DR. BLANC: They're considering in utero exposure.

DR. FUCALORO: But there are some things a mother is exposed to that can damage the uterus in some fashion -- rather the fetus in some fashion, but her child, a newborn, may not be exposed. It would also be considered in this group.

DR. BLANC: That's what they're saying.

DR. FUCALORO: That's what you're getting at. Yeah. I think it has to be thought through. Is that what you mean? That's what you're asking.

DR. BLANC: That's what I'm asking, and their answer is yes.

CHAIRMAN FROINES: You realize that also, I mean, Congress, the House of Representatives, just passed a law yesterday --

DR. FUCALORO: That's right.

CHAIRMAN FROINES: -- mandating that damage to the fetus was considered an illegal act.

DR. FUCALORO: Well --

CHAIRMAN FROINES: And so it obviously has implications for issues of choice, so that this -- taking this position isn't trivial as a matter of public policy.

DR. FUCALORO: Yeah. That's why I mentioned it.

DR. BLANC: See, for lead, it's not an issue. For mercury it's not an issue because whether or not there would be -- clearly there are effects in utero, but there are clearly effects to neonates, so that's not an issue.

Carbon monoxide is not an issue because yes, there's even more hemoglobin in your fetus, but there's still an awful lot of fetal hemoglobin when you're a very early neonate. That's not an issue. But for some of the things you're talking about where the evidence is

just teratogenic toxicity, then you're really making the argument, and we're not really talking about central nervous system sensitivity which goes on for months and years of childhood, then, you know, the DES kind of argument, which you're very explicit about in your introduction.

And I think it's a bit of a murky area, in fact. I'm not sure that I -- I'm not sure that I accept your argument logically that it's -- that it logically flows, that that means -- that that is the same as having newborn or childhood sensitivity or susceptibility because the adult -- I mean, the damaged child who survives to adulthood -- the fetus has survived to infancy and childhood and then to adulthood, but the susceptibility is not in childhood or in infancy.

And the whole piece of legislation, as I read it, never uses the word "fetus" or "fetal" or "prenatal" anywhere.

DR. MARTY: Well, let me just give you another example. George is kicking me. But things that result in --

DR. FUCALORO: Excuse me. Why is he kicking you?

DR. BLANC: That's between them.

DR. MARTY: Because he wants me to stop. If something impacts birth weight, for example -- birth weight is a good example. Low birth weight babies, there's a linear relationship between birth weight and infant mortality, and infant mortality I consider an effect that occurs only if you're an infant.

DR. FUCALORO: Do you mean linear, or do you mean there is a relationship?

DR. MARTY: It's pretty much linear. It's pretty much linear. And a lot of low birth weights, you know, generalize chemical stress. I think that's an important issue. If there's chemicals out there that do this, and you're breathing them, that's an impact.

DR. BLANC: Like it --

DR. MARTY: It's just -- it's different than terata. It's different than the production of terata.

DR. ALEXEEFF: Another point to make on this, other than the fact that I wasn't kicking her, is that --

DR. FUCALORO: It was accidental; right?

DR. ALEXEEFF: No. Is that the way -- and we could add this type of information to the document. The way we reviewed developmental toxicity, there's not complete concurrence in the effects. In other words, we can do an animal model, and we might get some effect,

but we're not sure if in humans it will be expressed as, for example, low birth weight. A lot of it has to do with the timing of the doses and the species that's used and some other factors.

The other issue is that since development doesn't stop at birth, or if there's early birth, then there's still development processes happening. And if all we have is the data of exposure in utero, we have to -- we look at that to see if, you know, it's likely to affect what's occurred.

Although, you mentioned thalidomide, that's not the only effect it has. It does have some neurotoxic effects as well. So we might -- I think what we'll have to do is we'll have to flesh out a few more reasons as to what we're taking into account, and I don't think we have, necessarily, an example where there is clear teratogenicity in utero, and postnatally it's clear there's no differential effect in children. I don't think we have that kind of example.

It's more like --

DR. BLANC: Well, I think --

DR. ALEXEEFF: There's little evidence. And what evidence shows that there's this differential effect between mother and fetus, and the rest of it is all, you know, less clear. And the concern is that, you

know, development continues, and they would be more susceptible.

DR. BLANC: Well, I think to the extent that you're talking about -- and you're a pediatrician, so I think you should respond to this perhaps. But to the extent that you've identified in utero effects, which are particularly notable in the last trimester, and you're certainly on much firmer ground to make some assumptions that, in fact, there would also be effects if newborns were exposed.

But to the extent that you're dealing with teratogenic effects, which require them to be fairly early in gestation, then I think you're much less able to make the kind of leap that you're making.

Let me ask another hierarch question: If you had two substances, one of which you had convincing data that could aggravate asthma and another which you had fairly convincing data that it could initiate asthma, in your hierarchy of issues, as I read your document, that substance which could tend to initiate asthma would be far more important; is that correct?

DR. MARTY: I'm not sure it would be far more important.

DR. BLANC: But it --

DR. MARTY: But it would definitely be

important. That's an important issue.

DR. BLANC: It's an irreversible effect, isn't it?

DR. MARTY: Yes, it is.

DR. BLANC: And then you said irreversible effects are more important than reversible effects?

DR. MARTY: Yes. Those have an important effect on your immune system. Those are important issues.

DR. BLANC: And in terms of something that could aggravate asthma versus something which could cause neural, developmental impairment, literally, the neurotoxin would be more important. It just doesn't effect.

DR. MARTY: You know, those kinds of issues are extremely difficult. Those questions are hard to answer.

DR. FUCALORO: But you have to answer them.

DR. MARTY: The prevalence of asthma is huge. There are so many people with asthma. You are impacting a lot of people when you have things that exacerbate asthma in the air. The neurotoxicants probably impact fewer people. But if I had my choice, I think I'd rather have asthma than developmental neurotoxicity. I mean, that's about all you can do to weight that kind of

an issue.

DR. FRIEDMAN: But even there, the question of aggravating asthma versus causing it, if it only caused it in one in 10,000 people exposed, but it aggravated severely all the people who had asthma, I think then the aggravation would be worse than the causation.

DR. BLANC: Well, I was actually asking the question in a simpler format. I wasn't -- if you assumed, I wasn't taking prevalence as the issue.

DR. FRIEDMAN: But you can't ignore prevalence.

DR. BLANC: No. You could take that as a separate weighting issue because in your document you talk about things that a matter, reversibility versus irreversibility. There's no real hierarchy that one can follow in terms of, you know, what matters. Clearly prevalence is one weighting. You have a lot of different things.

DR. MARTY: People have tried to develop such hierarchies. The U.S. EPA tried for years to develop hierarchy. Are you going to call a carcinogen worse than a neuro-toxicant and so forth? And they were unsuccessful. They just gave up. And it's just -- it's so difficult. Are you going to put a "No. 1" on carcinogens and No. 2 on -- you know, it's just a balancing act. You have to think about all kinds of

other issues that come into play, which is what we tried to do.

CHAIRMAN FROINES: Tony.

DR. FUCALORO: Yeah. Well, you certainly did some quantitative ranking using the scale you did in No. 2 and 3 at the beginning of this document relating to toxicity and exposure.

DR. MARTY: Yes.

DR. FUCALORO: Now, I recall a couple years ago when you brought before us the methodology you used to decide which chemicals you would investigate as a TAC, and you have a methodology which listed. And I thought it was a very good document. I don't have it any longer, unfortunately. I didn't bring it with me, if I do. But have you looked at that methodology?

DR. MARTY: Yes.

DR. FUCALORO: It seems to me this would be -- that would be a good start. Maybe you have already.

DR. MARTY: It actually was the starting point.

DR. FUCALORO: It actually was the starting point. All right. That's fine.

CHAIRMAN FROINES: I don't know how we are to resolve the issue of the in utero toxicity because Melanie knows that I feel the way Paul feels, and we've heard from Paul. So at least two of us have strong

reservations about the thalidomide example as an example of differential susceptibility, and I don't quite now how to resolve the issue. But it's a very troubling one and clearly has much broader policy implications to the degree that one accepts the current definition.

So I'm at a -- George and Melanie, I'm at a loss for how to proceed on that one. I suspect that one ought to get some legal counsel to ask something about the intent of the legislature with respect to children. I don't know whether -- I suspect we will not get any kind of answer that will be very definitive but --

DR. MARTY: We could --

CHAIRMAN FROINES: -- I don't have -- I mean, clearly we have a clear difference of opinion here that at least two of us hold relative to your point of view. And we haven't sort of polled the rest of the panel, but I don't know how to resolve it.

DR. BLANC: I think the first step is to have it explicated clearly in the document, because, actually, I can't really respond to it because it's not there for me -- there's no there there for me to respond to it subtextually. So you need to firmly elucidate what it is you're trying to do in that regard and then --

DR. MARTY: Then we can talk about it. And it

also helps to go through specific examples of the chemicals.

DR. FUCALORO: To the extent possible -- I think John's point is correct. I think you should try to uncover the original intent of the legislature, but to the extent -- I don't know if that's -- certainly they're still around, unlike the American founders, but -- so you might have a real chance to get some direction from them.

CHAIRMAN FROINES: Well, I also think that, going to the next step, that this is a particularly good discussion, and it illustrates the fact that there are a lot of issues that are really not as well defined in the document as they need to be in the long term. And so the issue of neurotoxicity is certainly one that requires subsequent follow up. This issue is another, and perhaps we'll identify others as we go along.

But that when this document is finished, hopefully it will be a document which is only about these issues, and all the other stuff that's in the current documents will be gone, the review of -- the review of the toxicity of the individual chemicals will be gone, and the specific criteria will be laid out, and then the relationship between the criteria and the evidentiary basis for a decision will be clear.

DR. BLANC: Actually, let me come back to another example which may help clarify for me what your thinking was. Let's take DES, not thalidomide. Let's say DES was an air pollutant. Where the effect were -- the exposure occurs in utero, the differential main toxicity is manifest in adulthood. Therefore, that would be something that you would not consider because it doesn't preferentially effect children at all or because it's -- because the exposure occurred in utero, you would include it?

DR. MARTY: We would include it.

DR. BLANC: Now, see. I think that's completely bizarre.

DR. MARTY: Well, let me explain why. Because DES does not have that impact if you're not a maturing organism. The only reason it's manifested as a teenager is because you were exposed in utero. If you were exposed when you were 16, it wouldn't have manifested the same toxicity.

DR. BLANC: But if you were exposed when you were an infant or a child --

DR. MARTY: I don't know. No one's done those -- no one's done those experiments with DES.

DR. BLANC: But there's no particular reason to think that it wouldn't work. Well, are you sure no

one's done that with animals?

DR. BYUS: With animals they've done that.

DR. MILLER: This is maybe changing it slightly, but from the neurotoxicity standpoint with which you're very interested, there is good evidence for a number of chemicals, particularly metals, that while the most severe effects occur during the earlier stages of development, that, in general, those correlate, if you can study them well enough as has been done with lead, to an effect that is also found in postnatal life.

DR. BLANC: No. I agree with that.

CHAIRMAN FROINES: We buy that. That's a given.

DR. BLANC: I don't think that that applies to the issue of vaginal cancer.

DR. MILLER: It doesn't. But what Melanie is saying is true it's certainly a number of areas where we don't know, perhaps, you know about the postnatal exposure because we don't have it. We don't have that to look at. Nobody's done those experiments.

CHAIRMAN FROINES: And so if it was an air pollutant -- if DES was an air pollutant and one was exposed to it throughout one's life, does it increase the risk of breast cancer and ovarian cancer because of its estrogenic nature? It could. So we don't really

know.

DR. MILLER: We don't know.

CHAIRMAN FROINES: But one could predict that it has hormonal-related cancer effects.

DR. BLANC: I was only asking the question to clarify your thinking, and I think I understand your thinking, which is that if something is a teratogen or has effects that are only -- can only be manifest with exposure in utero, even -- even were the only known effects to be seen in adulthood, you would consider that to be fair game under this legislative mandate.

DR. MARTY: We would.

DR. BLANC: All right. I understand your thinking.

And I would reiterate what John said, which is, A, get some legal counsel, and, B, make it very, very clear. And I think, by the way, that you may find in this document a brief section which uses examples of chemicals for which you're not even -- you're not remotely suggesting that they be addressed here because they either aren't air pollutants or, you know, it doesn't matter.

But for illustrative purposes, were they to be air pollutants, why they would have been something you would have looked at very closely would be very helpful.

DR. MARTY: Okay.

DR. BLANC: You know, radiation, for example, which you alluded to in the introduction.

DR. MARTY: Right.

CHAIRMAN FROINES: I think that you realize that you may have -- you've had public comments up to now, but a very large number of groups who have concerns about abortion, when they discover that this is in your document, may also have significant concerns, and that it may -- this may be opening a box that we all understand may occur, but it's -- it will -- it changes the nature of the discussion.

DR. BLANC: Because you're essentially saying, if I need to be even more explicit, you're saying that fetuses are the same as children or infants.

DR. MARTY: Well, we're saying that development starts at conception and goes through birth and out into adolescence, and we're not distinguishing development that occurs before birth with development that occurs after birth.

CHAIRMAN FROINES: But then we're going to -- then it's possible that when one gets into defining risk- based approaches for those chemicals, you will define -- you will define the risk associated with those events.

DR. MILLER: Not -- perhaps this is germane, but just as a point of reference, the field -- the developing field of pediatric environmental health has in general taken development from prior to birth through adolescence as the field, for whatever that's worth.

DR. MARTY: And actually in a minute when we talk about benzene, we're going to talk about pre-conceptual parental exposure.

CHAIRMAN FROINES: Right. I want to be on the record and say that I think that in utero exposure at various time frames can affect the health outcome of an individual throughout their lifetime, and I think there's increasing evidence to indicate that there is a whole series of health outcomes that may get impacted over a long period of time from in utero exposure. So it's a developing field, but this is a -- this is in relation to this particular law. That's the issue here.

DR. MARTY: Should we move on to the individual chemicals?

CHAIRMAN FROINES: Please.

DR. MARTY: I just thought I would go just in order that they're listed, which is alphabetical, through the first five that we proposed or suggested for listing and then through the remainder.

DR. FUCALORO: Is there a handout that covers

this?

DR. MARTY: The handouts are coming.

DR. FUCALORO: Oh. They are.

DR. MARTY: That's what Peter was asking me about.

Tom McDonald is a toxicologist at OEHHA. Tom is going to give the presentation on benzene. What we're going to try to do is summarize what evidence we considered to implicate a chemical as having a differential effect, and then I will summarize briefly comments we got on those chemicals and our responses, which all of the panel has had the comments and responses sent to them already. So it will be a brief summary.

DR. MCDONALD: Well, hello, everyone. The last discourse that this group had will certainly feed right into discussion here on benzene.

Benzene was placed in Tier 1 primarily because of suggestive evidence for differential susceptibility with respect to cancer. The evidence summarized in one slide here is the suggestive evidence of associations between parental exposures, both maternal and paternal, and childhood leukemia in some studies but not others, and there is some supportive animal data to support these epidemiological findings.

Also, there's a possible increased lifetime cancer risk from early life exposures to benzene relative to adult exposures, and that evidence comes from one set of inhalation studies in animals conducted by Malatoni et al. And there is indirect evidence from other leukemogens, namely radiation, such that we see early life exposures to radiation induce a greater excess of leukemia mortality compared to exposures occurring at, quote, "working age individuals."

Next slide, please. Just to briefly summarize that benzene also is considered a developmental toxicant. Benzene was listed as a developmental toxicant under Proposition 65 in 1997. And currently OEHHA is working to develop a maximum allowable daily intake level based on the developmental effects of benzene.

Since it is still likely that cancer will drive the regulatory effort --

CHAIRMAN FROINES: Can I interrupt? I hope that you guys can avoid doing what you just did. I want to know what is the science with the -- associated with benzene as a developmental toxicant? I don't give two hoots about what OEHHA did under Prop 65. The science is what we're talking about here, not about an agency decision. And so what happens replete throughout this

document is references to agency decisions, and I think that that doesn't make an argument that has any weight for me.

I want to know what is the scientific basis for a decision, not what did EPA say? What did OEHHA say? What did Joe -- Agency X say? I think that what happens is there gets to be this reliance that says if some agency says something is so, therefore, it must be so. And, as a scientist, I don't accept that whatsoever.

DR. MCDONALD: Okay. Just to respond that the developmental evidence was presented as a context that, you know, this is what's available. But the focus of the summary in the original draft was cancer, and I tried to discuss in more detail that evidence, and that's what I will continue to discuss here. There will be no more slides on developmental toxicity of benzene beyond this one.

Next slide, please.

CHAIRMAN FROINES: Well, is it -- is it a basis for your decision?

DR. MCDONALD: No.

CHAIRMAN FROINES: No. So we didn't really even need that slide, did we? So why do we have it then?

DR. MCDONALD: I was just --

DR. MARTY: I think that --

CHAIRMAN FROINES: I told Melanie that I wanted to have -- that you come and present the criteria for decision making and the basis for decision making. I don't want you to present information that did not serve as the basis for your decisions because we can't judge that.

We have to review what you think is the rationale for the decision, and that has to be what this panel can deal with. We can't deal with things that are not directly relevant to the question before us.

DR. MCDONALD: Okay.

CHAIRMAN FROINES: And I don't mean to be harsh about it, but we've been here for hours, and we're going to be here for hours and days more. And we have to really focus on the science associated with the decision making process within the context of your criteria.

DR. MARTY: Okay. Well, let's do that right now.

The evidence for differential susceptibility with early life exposures to benzene, it can be thought of in two categories, if you will. The paternal exposures to benzene and how it might relate to increases in childhood leukemia, as well as early life exposures, either in utero or postnatally that may

increase lifetime excess of cancer risk.

Next slide, please. With respect to benzene and childhood leukemia, there is suggestive evidence in some epidemiological studies, but not others, both from paternal exposures, that is, exposures to the father pre-conceptually, as well as maternal exposures, thus in utero. And I'd like to stress that this information will -- although suggestive, would be very difficult to establish a causal relationship between these two, you know for childhood leukemia and benzene.

I should note that there is some animal evidence that would support such associations, and that includes benzene exposure in vivo, which causes DNA damage to sperm, as well as transplacental genotoxicity, as well as transplacental altered hematopoiesis, which is believed by many to be an important mechanism in benzene to produce carcinogenesis.

Next slide, please. And oh. By the way, I have detailed slides of the epidemiological studies at the end if you care to go into those in more detail.

Early life exposures to benzene and increased lifetime leukemia risk, there's only one animal study on benzene that has exposed prior to weaning, and that is the Malatoni studies. Offspring that were exposed in utero through lactation and adulthood, that is, a total

of a 104-week exposure, resulted in greater incidence of -- relative to the exposures to the dams that were exposed for 85 weeks.

So I've shown here Zymbal gland, which is the most consistent tumor site found in both species of rodents commonly tested. You see the treated females from the offspring had a 12 percent tumor rate compared to controls which were zero percent. Whereas, the rate in the dams was 6 percent and the controls were 2 percent.

So this roughly means that a 20 percent increase in exposure time resulted in a twofold increase in tumor rate. And, as stated in the draft, we need to really do a detailed assessment to see if such an increased tumor rate can be explained by dose or whether there is some suggestion of a differential susceptibility.

Next slide, please. With respect to the human evidence in this question of lifetime leukemia risk, there is no direct studies which have looked at early life or childhood benzene exposure and lifetime excess of cancer risk. However, there is age-dependent evidence from other leukemogens. Of course, the biggest data sets are from radiation.

And just to note that radiation-induced

temporal patterns of leukemia have for decades been used to weight benzene-induced leukemia risk, including the current cancer potency estimate for the California TAC for benzene, and I can explain this in more detail if you'd like.

Next slide. If we look at the available evidence from radiation-induced leukemia with respect to age at exposure, we see a differential pattern such that exposures early in childhood cause a greater excess leukemia mortality than exposures occurring, say, during the working age of, say, 20 to 50, and that, of course, is, you know, the ages with which the cancer potency of benzene is based on.

And this is a period, you know, suggested by the radiation data of lowest susceptibility to leukemogenesis. So that concludes the core evidence.

DR. GLANTZ: This is --

DR. BYUS: Mechanistically, I mean, comparing benzene and radiation in terms of the mechanism --

DR. MCDONALD: Yeah.

DR. BYUS: -- by which it might induce cancer, what do they think about that?

DR. MCDONALD: Well, I think it's more just an inherent. It's an inherent -- it's trying to get at the inherent properties of the turnover of bone marrow and

the response to bone marrow to DNA damage.

DR. BYUS: So there's some similarity in the mechanism?

DR. MCDONALD: Yeah. There's lots of comparative data. For example, after radiation exposure, excess leukemia rises quite rapidly within five to ten years following exposure, and then, unlike other cancers, comes back to background rates by about 30 years following exposure. Now, that is very consistent with several classes of chemotherapeutic agents as well as consistent with what we see in benzene-exposed leukemia cohorts from benzene-exposed workers.

So there is lots of data to suggest very similar temporal patterns between the two responses between these two types, chemical versus radiation. So I think it's a reasonable -- biologically, it's a reasonable argument to make.

DR. GLANTZ: But -- well, that was actually -- I was very confused by that, too, and, I mean, were you saying in the document that benzene -- that there was some interaction between benzene and radiation exposure, or were you just saying that you think that benzene exposure behaves, in terms of effects on risks, behaves similarly to radiation?

DR. MARTY: That has been the pattern with other analysis of temporal responses, yes.

DR. GLANTZ: And could you explain again why you would expect that to be the case? What's the affirmative evidence that benzene exposure should act like radiation exposure?

DR. MCDONALD: Well -- sure.

DR. MARTY: I think what we're trying to say is that other known leukemogens, including chemotherapeutic agents and radiation, exhibit this wavelike pattern of susceptibility to leukemia, and that that points to something innate about the hematopoietic system in terms of its sensitivity to leukemogens at those various ages.

DR. GLANTZ: I see.

DR. MARTY: If that holds true for benzene, then you would be expect that for benzene.

DR. BYUS: I still find, you know --

DR. GLANTZ: Yeah. I think that's --

DR. BYUS: I could still see chemotherapy and radiation causing DNA damage directly, mutation. It's hard to see that for benzene mechanistically. But I see -- I understand what you're saying about the turnover of the marrow and --

DR. MARTY: It's genotoxic metabolites of benzene.

DR. BYUS: All right.

DR. MARTY: Yes.

DR. BYUS: Okay. So there are genotoxic metabolites in --

DR. MCDONALD: Yes. Benzene is a very strong clastogen.

DR. BYUS: That's the answer.

DR. MCDONALD: Yeah.

DR. BLANC: But, in fact, the document -- the -- I mean, I might have missed this, but in the section on benzene itself, is the analogy with the post chemotherapy incidence of stem cell malignancy, bone marrow malignancy in terms of dose response for children treated for malignancy versus dose response for adults treated for malignancy explicated in the text of the document. The radiation stuff is there.

DR. MCDONALD: Yes. There are several published studies describing this temporal pattern.

DR. BLANC: There's two temporal patterns you're describing.

DR. MCDONALD: Yes.

DR. BLANC: I'm not arguing about the -- the germane issue is not the temporal pattern.

DR. MCDONALD: Correct.

DR. BLANC: There's an increase in incidence

five to ten years afterwards where some falls off, because that's true for anyone at any age.

DR. MCDONALD: Yes.

DR. BLANC: But is there data that shows that per milligram -- per square meter of exposure to -- it says "platinum."

DR. MCDONALD: Yeah. I'm not aware of such date, and such data would be complicated by the fact that children often are given, I believe, higher doses of chemotherapeutic agents because they can tolerate them.

DR. BLANC: Yeah. That's what I said. I'm not an expert.

DR. MCDONALD: I'm not aware of an analysis that shows increased response to chemotherapeutics by age. There may be.

DR. BLANC: Is there?

DR. FUCALORO: Can I just make a small, technical point? Your unit risk factor in the benzene report is probably wrong by a factor of two. I think. Compare it with some of the other data. Unless your table is wrong.

DR. MCDONALD: Which?

DR. FUCALORO: I think you recorded CCL 4 as carbon tetrachloride. I know it's off point, and I'm

sorry, Mr. Chairman, but I'm trying to do some calculations, and I want to use the right number.

DR. MCDONALD: Well, the unit risk factor in inverse micrograms per meter cubed is 2.9 times 10 to the minus 5.

DR. FUCALORO: That's what you have in the document.

DR. MCDONALD: That's correct.

DR. FUCALORO: Yeah. And in the table it's 5.9.

DR. MCDONALD: Okay. We'll --

DR. FUCALORO: So one of those are wrong. Maybe both of them are. I like to open up all possibilities.

DR. BLANC: Let me just follow up on my previous question. The fact that there's a technical response to things which cause leukemia that's much shorter latency than -- for most other forms of cancer is irrelevant to the discussion here. That bears no relevancy at all to the issue of childhood susceptibility, does it? Or did I miss something?

The only issue is whether the children would be more sensitive or more responsive to an equivalent dose of leukemogenic agent.

DR. MCDONALD: Right. We're just trying to get

at some picture of the inherent response of the bone marrow and the only --

DR. BLANC: Again, but the first point has no relevance to our argument here.

DR. MCDONALD: Well, I've shown age-specific data on radiation. Did I miss something?

DR. MARTY: I don't understand the question.

DR. BLANC: There are two temporal issues. One is that, yes, it is true that things which cause leukemia tend to have a shorter latency, and then you have a fall off to background levels.

DR. MARTY: Right.

DR. BLANC: That has no relevancy to our discussion here.

DR. MARTY: Correct.

DR. BLANC: What has relevancy to our discussion here is if you exposed a three year old to one rad of radiation, would they have a greater incidence of leukemia than a 20 year old exposed to one rad of radiation?

DR. MARTY: Yes.

DR. BLANC: And then I asked the question, is there similar data for chemotherapeutic agents, and the answer I got was no, not that you're aware of.

DR. MCDONALD: Correct. But that -- yeah.

DR. MARTY: We're going to look at that because I was under the impression that there are.

DR. MCDONALD: I'm just not aware of them.

DR. MARTY: It's the most common, secondary cancer following treatment in childhood for other cancers. Whether there's data showing on a per milligram, per kilogram body weight basis, we can dig around for that, but I am remembering that there are those data, so we can look at that.

CHAIRMAN FROINES: Am I correct to assume that we've heard the basis for the decision or -- which is a series of articles -- a series of sort of arguments that are --

DR. MCDONALD: Yes.

CHAIRMAN FROINES: -- somewhat indirect, or is there coming a more definitive statement?

DR. MARTY: We have some slides on the epi studies that indicated parental exposure that may be associated with leukemia risks. But that you pretty much have heard the two points.

DR. MCDONALD: Right. If you want me to go into details about the epidemiological studies of parents and childhood leukemia, then we can go into the specifics.

CHAIRMAN FROINES: I --

DR. MARTY: Let's go through them

DR. MCDONALD: Would you like to go through it?

CHAIRMAN FROINES: I don't know what the panel would like.

DR. BLANC: Maybe what we could do is hold that in abeyance and come back to it because I think we need to have some sense of the substances, one as opposed to the other, and it's already a quarter to 3:00. And we do have those on your -- there on your handout --

DR. MCDONALD: Yeah.

DR. BLANC: -- so we can come back to them without seeing the slides, if we wanted to then at that point to compare --

DR. MCDONALD: Whatever the panel would like.

DR. BLANC: Mr. Chair, would that be okay?

CHAIRMAN FROINES: Yes. I think -- from my standpoint, I think the evidence is extremely weak for benzene at this point given these arguments.

DR. BLANC: Well, can we just hear some of the others? Let's get some comparison. I know you're put in the position where you have to name five things. So it may be that this is very weak data. Obviously you felt the data were even weaker for one of the others, but let us just get a sense of where you're coming from. For the group, it's very important I think --

DR. MARTY: Okay.

DR. BLANC: -- to get comparative cases.

DR. MARTY: Okay. Do you want me to hold off on the comments and responses --

CHAIRMAN FROINES: Yeah.

DR. MARTY: -- on benzene?

CHAIRMAN FROINES: Let me ask the panel about that. I asked Melanie if she would be prepared to address comments because for most of us the comments are extremely important. So she was prepared to respond -- to give a response to comments. And so the question is, should we move on at this point and take on some other chemicals --

DR. GLANTZ: Yeah. I think -- I think --

CHAIRMAN FROINES: Or would you like to hear the comments -- the response to comments?

DR. GLANTZ: I agree with Paul. I think it would be really helpful to go through the other chemicals, or at least some of them, and then we can come back if there's time and deal with the comments.

CHAIRMAN FROINES: Okay.

DR. GLANTZ: Because we -- we read them.

DR. MARTY: You read them. Okay.

DR. GLANTZ: Or at least I read them. I don't know about everybody else.

DR. MARTY: Let's go to formaldehyde. Stan.

Andy, we're going to go to formaldehyde.

DR. DAWSON: Good afternoon.

DR. GLANTZ: Why are you quaking?

DR. DAWSON: Why am I -- well, after the little interchange. I'm here to defend formaldehyde.

DR. GLANTZ: We're very nice.

DR. DAWSON: Formaldehyde was chosen for Tier 1 based on chronic respiratory response or effects, including allergic effects. It has the potential to exacerbate asthma, and you can see measured impacts on lung function in children, chronic respiratory response.

Some indication that children may be more sensitive to long function changes than adults at low level exposures and carcinogenicity is a concern.

Actually, just as an overview of the one study, this study here compares disease response of children and adults directly. Three other studies support this one, suggesting an effect of formaldehyde at even lower exposures.

CHAIRMAN FROINES: This is the only one that looks like it has a differential; correct?

DR. DAWSON: Yes, this is the only one.

CHAIRMAN FROINES: The other three don't do that.

DR. DAWSON: That's right.

So this is the Krzyzanowski et al., with Quackenboss and Mike Lebowitz. Chronic respiratory effects of indoor formaldehyde exposure, chronic respiratory symptoms were reported and diagnosed. This first slide is just a description of this study. And lung function was obtained by PEFR, peak expiratory flow rate.

There was information on tobacco education and NO2 in almost 300 children, 600 adults in 200 households, age 5 to 15 years, carried out in Tucson, Arizona. And the mean for formaldehyde is 26 ppb. And they study grouped individuals by less than 40 -- between 40 and 60 and above 60.

Results: First of all, the disease and symptoms, prevalence of asthma and bronchitis -- chronic bronchitis was significantly greater for formaldehyde above 60 ppb. This is a patent disease now, and P values there were much more significant for the chronic bronchitis than for the asthma. And the kitchen levels of formaldehyde bore the closest fit.

The reported symptoms of the children from the questionnaires were not related to formaldehyde. And there are a bunch of symptoms that were asked for, and neither symptoms nor actual disease were significant.

That is doctor-diagnosed disease were significant for adults. Yet there was a higher end, remember, in the adults. So we should have seen more power to see an effect.

Next, the results for the peak expiratory flow rate which is a measure of general lung function. My understanding it's not just the airway size themselves. It also includes the compliance of the lung. The a.m. and p.m. PEFRs declined linearly.

DR. MARTY: That's morning and afternoon. They tested at four time points during the day.

DR. DAWSON: Yes. And it was equivalent to a 22 percent decline at 50 ppb, and that was just significant. The PEFR declined only in the a.m. in adults, and there was a very much smaller effect. And this study did control, to a good degree, for the effect of possible confounders.

Next. The next study, which overlaps somewhat but was only on children, was Garrett et al., the increased risk of allergy in children due to formaldehyde exposure in homes. It measured atopy, asthma and respiratory symptoms; eighty children, fifty-three of whom were asthmatic in 43 households. Mean age around 10 years, range 7 to 14 years. This was in a coal mining town in -- fairly near two different

mines in Victoria, Australia.

Median: Formaldehyde is 12.6 ppb with a maximum of around 100, and again there were three exposure categories.

The results: There was a significant increase in the adjusted odds ratio for atopy. 1.4 was the ratio per 8 ppb increase in formaldehyde level. There was more severe sensitization with formaldehyde increase as well. There was no significant increase in adjusted odds ratio for asthma or respiratory symptoms, but they were more frequent in children with higher exposures. And the adjustment was for parental asthma status.

DR. FRIEDMAN: Did they look for any other possible parental confounders like parental smoking or socioeconomic status?

DR. MARTY: I'm pretty sure they looked at parental smoking. I don't recall anything about socioeconomic. Presumably, it would be relative in a coal town. I assume it would be relatively whole in that respect.

Another supporting study is Franklin et al. This is raised, exhaled NO in healthy children is associated with domestic formaldehyde levels. Exhaled nitric oxide for lower airway inflammation is a marker for lower airway inflammation. They also did spirometry

and skin prick.

There were 200 healthy children, age 6 to 13. This is in Perth, Australia, the other side of the continent, and they divided formaldehyde into two groups at 50 ppb.

The exhaled formaldehyde was greater. This is the results. I'm sorry. Exhaled NO is greater in homes with the formaldehyde greater than ppb, and the measurement, just NO, was 16 versus 9 ppb. This is significant after controlling for all other variables and regression at quite a significant level, .002, and this was found to be independent of atopy.

Wantke et al., another supporting study, "Exposure to gaseous formaldehyde induces IGE mediated in sensitization in formaldehyde in school children." Specific IGE by rast and symptoms were looked at. Sixty children in three classes before and after a move of the classrooms from a higher level to a lower level of formaldehyde. Mean age was very close to eight years. All the kids were very close to eight years, one grade level, in Vienna, Austria.

And notice the formaldehyde levels here in the one class that went from 75 down to 29 and 69 to 23 and 43 to 26, so they were down by a factor of three or two.

Results.

DR. GLANTZ: If you could just -- one thing I don't understand there is when you say formaldehyde exposure -- if you back up one slide -- increased sensitization to formaldehyde, I don't -- so are you saying if they're exposed to formaldehyde once, then they become more sensitive to formaldehyde on subsequent exposures? Is that what that means?

DR. DAWSON: In the title?

DR. GLANTZ: Yeah. I don't quite understand what you're saying.

DR. DAWSON: Exposure to gases induces IGE.

DR. GLANTZ: Well, is that what you're saying happens?

DR. DAWSON: This is the author's title, "Exposure to Gaseous Formaldehyde Induces IGE Mediated in Sensitization." That's what their claim is.

DR. GLANTZ: So you're --

CHAIRMAN FROINES: He's asking what that means.

DR. GLANTZ: Yeah.

DR. MARTY: I think that the reason we're concerned about that is that, typically, people have thought of formaldehyde sensitization as occurring at high occupational exposures, and, therefore, it's really an adult problem, not a child problem.

And this paper is measuring

formaldehyde-specific IGE in kids who were exposed at commonly encountered indoor air levels. That to me was significant because it kind of bucks the tide of this idea that you have to have real high exposures to find any evidence of sensitization. Whether it's clinically different or not is a different issue.

DR. GLANTZ: But the question I'm just asking, when you talk about sensitization, is that saying that you get sensitized -- you get exposed to formaldehyde, that sensitizes you so the next time you're exposed to formaldehyde, you get a bigger effect? Or are you saying -- is this a measure -- are you just saying that these kids were responsive to low doses of formaldehyde?

DR. MARTY: It's the latter. We're saying they were responsive to low doses. We're not sure if you took these kids and gave them various exposures how --

DR. BYUS: It's the classic sensitization to make IGE after the first exposure such that when they're exposed again, there's the antibody there, and it binds to it and gives you the massive response.

DR. GLANTZ: Okay.

CHAIRMAN FROINES: I assume this is just a cross-sectional study where they took a population of kids, measured their IGE and measured their formaldehyde levels.

DR. DAWSON: Right.

DR. MARTY: It was specific kids in a school district in Vienna, and they were interested in it because the reason they moved the kids was because they had high concentrations of formaldehyde, and they were all in these little rooms with paneled particle board, and then they moved them out to a different set of classrooms and took the opportunity of measuring the IGE when they --

DR. DAWSON: Of course they came to the --

DR. BLANC: But their IGE should have stayed the same, virtually.

DR. MARTY: Well, I think the -- the IGE dropped after the children were moved to a lower formaldehyde concentration.

DR. BLANC: It's not clear to me that it would have. Why would it have dropped?

DR. DAWSON: Well, I think that --

DR. BLANC: Your symptoms may drop, which they didn't.

DR. DAWSON: Yeah.

DR. BLANC: Well, none of that -- I mean, this isn't particularly relevant to children being more likely to become more sensitized than adults, of course. But perhaps we can go back to -- just a question about

the main study that drove all of this is the Krzyzanowski study?

DR. MARTY: Right.

DR. BLANC: That's -- everything else is ancillary, supportive in your view.

DR. DAWSON: Right.

DR. MARTY: Supporting that you can measure formaldehyde respiratory health impacts at low levels, that you can find formaldehyde-specific IGE even at low levels in kids. There is not -- there were not comparisons to adults in these other studies.

DR. BLANC: So in the Krzyzanowski study, the linear relationship cross-sectionally between peak expiratory flow and the measured formaldehyde levels, in your slide where you say there was a linear decline, I haven't gone back to read the article myself. I'm just trying to understand what you were trying to say.

There was a dose response relationship cross-sectionally between peak flow in all children as a group, which included some subset of them that had asthma or didn't have asthma.

DR. DAWSON: Right.

DR. BLANC: So it wasn't a study that looked at whether children with asthma were more responsive to formaldehyde.

DR. MARTY: Correct. That's right.

DR. BLANC: So, in fact, it really is just a study of the irritant effects of formaldehyde insofar as they're just looking at -- if that's, in fact, the explanation of the cross-sectional relationship that we see.

DR. MARTY: Yes. It -- yes.

DR. BLANC: So you don't have data that shows that asthmatics exposed to formaldehyde have a bigger response than non-asthmatics.

DR. MARTY: That's right.

DR. DAWSON: Not in children.

DR. MARTY: As you well know, the data on formaldehyde-induced exacerbation of asthma are mixed. Some studies have said yes. Some studies have said no.

DR. BLANC: Okay. So I just want to make sure that I understand what it is that you're arguing. Because the implication, the one we just -- in the earlier discussion could have been interpreted differently, so I want to make sure that I understand what it is that you're trying to say here.

So this is for -- and when we go down from our generic arguments to the specific chemicals, this is an example of a chemical which, based on its irritant effects, the argument would be that -- in fact, the

argument here is not, in fact, anything to do with asthma. It's just that the irritant effects of formaldehyde you're arguing are greater in children than they are in adults.

DR. MARTY: That's the main argument, yes.

DR. BLANC: And having nothing at all to do with asthma at all. So it's not related to the argument of how many children have asthma in the population?

DR. MARTY: Well, we used the potential since I'm not completely convinced that asthmatics wouldn't respond more than non-asthmatics to formaldehyde. We use that as sort of another little piece of information. But the real crux of the issue is this paper and the impacts on measures of respiratory function being greater in the kids in the study than in the adults. So yes.

DR. FUCALORO: So in your main text when you say "summary of potential for differential effects" means there may not be differential effects because you say "including cellular" and "exacerbation of asthma."

DR. MARTY: Right. That's right. Some of those -- some of the effects we list have more weight because the data are better and stronger. In the case of formaldehyde --

DR. BLANC: The argument is that children are

more likely to have the irritant effects of formaldehyde --

DR. MARTY: Yes.

DR. BLANC: -- at a dose more than for any other irritant. Preferentially more, except for maybe some other irritant that's in the list of 11. But, in general, of all the irritants that one could look at, formaldehyde is one at which -- given the levels of ambient exposure, children would be more likely to have an exaggerated irritant response --

DR. MARTY: Yes.

DR. BLANC: -- than adults even taking into account their greater respiratory rate, et cetera, et cetera, et cetera.

DR. MARTY: Yes. That's the crux of the --

DR. BLANC: And that's based on the Krzyzanowski study.

DR. MARTY: Right.

DR. BLANC: I'm just trying to understand the argument. Okay.

DR. DAWSON: And then I would just add that these are quite low levels of concentrations we're talking about.

DR. BLANC: I don't necessarily think that any of the ancillary studies are that relevant to the

argument you're making since none of them are looking at children versus adults, and the IGE argument is so far off base because that's not the argument you're trying to make. You're not trying to say that children are preferentially sensitized to formaldehyde either because the whole issue of sensitization is a big can of worms that you probably don't want to get into.

You're certainly on much firmer ground when you talk about irritant effects of formaldehydes than when you talk about sensitization since even an occupational population is included. It's exceedingly difficult to demonstrate specific sensitization to formaldehyde which makes the Vienna data seem very suspect since it's very hard to show specific IGE reliably for formaldehyde.

DR. DAWSON: Well, just to respond to the one key study in Vienna, again, I did look that up. The rast values do drop when they move to the classroom. In three months, the rast drops significantly.

DR. BLANC: Yeah. I understand. But what I'm saying is it's difficult to understand what that rast is because, technically, looking at a rast for formaldehyde, it's a very, very -- it's one of those murky, difficult, controversial areas is all I'm trying to point out. There's a lot of pitfalls.

DR. DAWSON: And I hope I did mention that the

NO is -- the authors believed is a measure of inflammation in the lower airways.

DR. BLANC: Right. That's just not a study that has anything to do with whether the children have more inflammation that adults. Nobody's arguing that formaldehyde is not a pro-inflammatory irritant.

DR. MARTY: Okay.

DR. DAWSON: But, see, these are at low levels. Very -- yeah.

DR. GLANTZ: Well, no one is arguing with that either.

DR. BLANC: Yeah. That's not the point.

DR. MARTY: The other -- when you read the document, we also do mention that it is a carcinogen.

DR. BLANC: Yeah. I know. I know.

DR. MARTY: It's a genotoxic carcinogen. That's another reason to be worried about early exposure.

DR. BLANC: Even though it's not exactly in order, I think the chemicals are so related it would be very interesting to hear, in light of your formaldehyde presentation, your acrolein presentation, one juxtaposed against the other.

DR. MARTY: We could do that.

CHAIRMAN FROINES: I don't think the

carcinogenesis argument any relevance, unless you're prepared to state just what it is.

DR. MARTY: Only that there is concern among lots of scientists that genotoxic carcinogens may be bad actors if you're exposed early in life. That's the concern. We didn't discuss it in the document other than to mention it. We didn't want to get into this argument over that specific issue since we are working on that in a separate program and don't have all of the information we'd like to have yet to develop that argument.

MR. ALEXEEFF: It's just a little bit of an aside -- George Alexeeff. We have a separate project where we're developing guidelines for assessing preferential carcinogenicity in children versus adults. That's something we'll probably bring back. We'll probably share it with this panel even though it's not directly part of this project, but eventually it will be part of it because it'll be part of the guidelines ultimately on how we do those things.

CHAIRMAN FROINES: Well, I think that it will be interesting. I think that short of an evidentiary basis, there are -- one has to decide where are the limits to speculation and a two sentence statement that says "Genotoxic carcinogens may have relevance to kids,"

may be entirely correct, but that's reaching a pretty high level of speculation with no evidentiary basis associated with it. That's all my point is.

It's not to quarrel. But you might not be correct. But it's hard for us to make a decision based on something like that.

DR. MARTY: Should we go to acrolein?

CHAIRMAN FROINES: Sure.

DR. MARTY: Judy Polakoff is going to present the information on acrolein.

MS. POLAKOFF: Okay. Acrolein was placed in Tier 2 because data indicate that ambient concentrations are above the chronic REL. Data suggests that acrolein may exacerbate asthma. And exposure to various pollutants, particularly reactive irritants, for example, aldehydes, can increase bronchial responsiveness to allergin stimulation or bronchial reactivity.

DR. MARTY: I'd like to add that it ranked first in our prioritization and had the highest ratio by a long shot of --

CHAIRMAN FROINES: Can I make one comment?

DR. MARTY: Sure.

CHAIRMAN FROINES: I'd just like to say I think that presentation is great. It's very succinct.

DR. ATKINSON: Okay. I have a question on the ambient concentration.

DR. GLANTZ: But he hates it.

MS. POLAKOFF: Okay.

CHAIRMAN FROINES: We give and take it away.

DR. GLANTZ: Are you having fun yet?

MS. POLAKOFF: So much.

DR. ATKINSON: The ambient air concentrations that you give for acrolein seem horrendously high --

MS. POLAKOFF: Well, we're going to get to that. We'll get to that.

DR. ATKINSON: At least with respect to what's being measured on -- or what was last measured in L.A.

MS. POLAKOFF: Okay. I'm going to get to that.

DR. ATKINSON: I mean, the data I've got from what looked like the most recent comprehensive study in L.A., which was -- admittedly it was 1993 data and published in '96, but it had the -- a whole bunch of carbonator compounds, and acrolein was an upper limit that was a factor of 100 less than formaldehyde.

DR. FUCALORO: Less than formaldehyde?

DR. ATKINSON: Much less. Yeah. Unless you're sitting somewhere, I assume, by a place which is emitting acrolein, a direct emission place, and not a vehicle, I don't see how it could be higher than

formaldehyde. I mean, if you look vehicle exhaust, both diesel and light duty, acrolein is significantly less than formaldehyde as an emission.

DR. MARTY: We have some information on other pieces of data that we found on acrolein measurement and model concentrations.

DR. ATKINSON: Yeah.

CHAIRMAN FROINES: Wait a second. Taking the prerogative of the chair, why don't we give her a chance to present some data, then Roger can quarrel with it, but let's have her give her statement and then --

DR. ATKINSON: Okay.

DR. MARTY: Andy, could you go back?

CHAIRMAN FROINES: Who published -- who's work is that?

DR. ATKINSON: This is Grandjean. It was published in '96. This is the last recent one with a whole bunch with acrolein.

I mean, your document actually says there's little data on acrolein.

DR. MARTY: Yeah. Andy, can we have the next slide. Sorry.

DR. ATKINSON: Sorry.

MS. POLAKOFF: Let me start by saying that acrolein is extremely difficult to measure. The Air

Resources Board has very little exposure data for us on acrolein, and the staff that we've spoken to have, you know, indicated that they don't have a lot of confidence in many of the measurements that are out there because it is so difficult to measure.

Now, having said that, these are the values that we found in the literature.

Andy, if you could do the next slide.

Here's also concentrations from cigarette smoke.

DR. MARTY: Can I add something there, too? When talking with ARB with Mike Pore, his concern about their measurements of acrolein were that they were underestimating because of the reactivity of acrolein and the methods they were using for sampling.

DR. ATKINSON: Okay.

CHAIRMAN FROINES: Could you go back to that just for a second? So that the California data are the top three?

MS. POLAKOFF: Yeah. The first two studies, they're very small. The first two are really small. The first one was 13 outdoor measurements. CARB took that data from Woodland California, and many of the measurements, I think, were below the level of detection, so that it's just a few numbers there. It's

not -- they're not really confident in those data I have to say.

CHAIRMAN FROINES: What does this paper say, Roger?

DR. ATKINSON: The paper I've got says that acrolein was observed in every measurement. There was 32 measurements, but in each case it was very close to their detection limit, and they put a number of less or equal to 0.04 ppb. And that was a --

DR. FUCALORO: 0.04?

DR. ATKINSON: Yeah. And formaldehyde was 5.3. There's an average of 32 measurements, and I think they were taken at four stations in L.A., Long Beach, Azusa, Claremont was one. I can't remember the other one.

DR. GLANTZ: What does that convert to in micrograms.

DR. ATKINSON: You multiply by roughly a factor of two, so it's about .1. Less or equal to is the way it was written in the paper.

DR. FUCALORO: So a hundred times different -- a thousand times different.

DR. ATKINSON: A hundred.

DR. BLANC: But, in all fairness, you have the California Air Resources Board data that they're presenting to us disagrees with that and is within the

range of U.S. EPA estimate, roughly.

DR. ATKINSON: Yeah. I mean, don't forget those data are not exactly -- apart from the second California one, the first one is 1990 data. And I suspect that the numbers are going down. At least emissions from vehicles are probably going down.

DR. FUCALORO: Well, isn't the 14.3, that is the U.S. -- I am sorry.

DR. ATKINSON: I don't know.

DR. FUCALORO: It's U.S. EPA data, at least by looking at that slide.

DR. FUCALORO: To 1980.

DR. ATKINSON: 1961 to 1980, yeah.

DR. BLANC: Well, there's a lot of exposure out there anyway, in your view?

MS. POLAKOFF: Yes.

DR. MARTY: Yes.

CHAIRMAN FROINES: Both as a primary pollutant -- in terms of primary emissions but also as an atmospheric chemistry product from butadiene?

DR. ATKINSON: Well, that's the only thing that forms it. I mean, formaldehyde is formed from every VOC, essentially.

MS. POLAKOFF: One more, Andy. Thanks.

U.S. EPA did extensive modeling work as part of

their cumulative exposure project, and they have modeling data for 148 hazardous air pollutants, including acrolein. And from that data, it's estimated that the annual, average ambient concentration of acrolein in California is 0.15 micrograms per cubic meter.

DR. GLANTZ: That's about what Roger said.

DR. FUCALORO: Yeah.

MS. POLAKOFF: Okay. Pratt et al., did a study examining the SEP data, the 1990 data, and did a study for Minnesota using the model data and some monitoring data looking at air toxics in Minnesota. They used a hazard quotient approach and compared exposure data. They used the modeling data from U.S. EPA, as well as monitoring data where they had it, and they compared that exposure data to cancer and non-cancer health benchmark values.

They only had modeling data for acrolein. They looked at over 1,200 census tracts in Minnesota and found out that for 70 percent of the census tracts studied, 70 percent of the census tracts exceeded the benchmark for acrolein.

Next slide. They also estimated a screening level total hazard index by summing all of the non-cancer hazard quotients over all endpoints. And

acrolein was by far the most important contributor to the non-cancer hazard index. Eighty-nine percent of the risk was attributed to acrolein. The next highest chemical was formaldehyde at 6 percent, and each of the other pollutants accounted for less than 1 percent.

And where they could compare their modeling data with the monitoring date, they found that the tendency was to under-predict measure values, which is what Melanie had mentioned before from ARB.

Next slide. Although there is no direct evidence of a link between acrolein exposure and asthma, the data do suggest that acrolein may exacerbate asthma in humans.

Next slide. This study was conducted in guinea pigs. The authors were looking at leukotrienes and acrolein-induced bronchial hyper responsiveness. The reason that they're looking at leukotrienes is that in airways, leukotrienes active mucous secretion and smooth muscle contraction and are thought to be important in the pathophysiology of asthma. So they wanted to see if they blocked leukotriene receptors with an antagonist or if they blocked the synthesis of leukotrienes, whether this would diminish the acrolein-induced broncho-responsiveness in guinea pigs.

And they also wanted to measure concentrations

of a specific leukotriene, the LTC 4, to see if it was -- if concentrations increased in lavage fluid if they found an increase in falling acrolein exposure.

Okay. And this slide along the Y axis a specific pulmonary resistance, and along the X axis is time. These two graphs could actually be superimposed on each other. On the Y axis, the scales are the same. They're just separated out for clarity I think. That's how the authors did it.

So in this part of the experiment, guinea pigs were exposed to 1.3 part per million acrolein for two hours, and then the graph shows broncho-constriction immediately following acrolein exposure. The top bar -- the top line with the open circles is just acrolein. And so acrolein alone, you see, increases specific area resistance, and this effect lasts about an hour.

Underneath it is the effect if the animals are given either the leukotriene receptor antagonist or the synthesis inhibitors prior to acrolein exposure, the effect is diminished, or at least it's delayed in some of the cases.

DR. BYUS: It goes up in the control, too, doesn't it? Did they give the control?

MS. POLAKOFF: The control is really just the --

DR. BYUS: No inhibitors?

MS. POLAKOFF: No inhibitors. Right. It's just acrolein by itself which is the top one.

DR. BYUS: No. I mean the lower panel, the control, did that get the inhibitors?

MS. POLAKOFF: The lower two -- the lower two are with synthesis inhibitors. Correct.

DR. BYUS: Both of them; right?

MS. POLAKOFF: Yeah. Different inhibitors.

DR. BYUS: It went up?

MS. POLAKOFF: One of them kind of delayed, and one of them diminished.

DR. BYUS: But the control in the lower panel went up when they gave the inhibitor without acrolein.

MS. POLAKOFF: They don't have it without -- all the animals are given acrolein. It's just whether or not they're given it before the acrolein exposure.

DR. BYUS: I'm just saying the lower -- in Panel B, the control, which I assume is the solid -- is the triangles, solid triangles, and was given inhibitor, two, leukotriene synthesis, that also increased airway resistance.

DR. MARTY: Actually, those animals were given acrolein after being given the inhibitor. So all four of those lines, the animals were being exposed to

acrolein.

DR. BYUS: Oh, all right. Okay.

MS. POLAKOFF: Sorry.

DR. BYUS: Sorry. No problem. It's what you call the controls that's always confusing. We always call them something different.

DR. MARTY: The control is actually the treated.

DR. BYUS: Okay. Okay. Okay.

MS. POLAKOFF: Okay. In this slide, the Y axis is the effective dose 200 or the concentration of acetylcholine that causes a doubling of the specific airway resistance. So this is the dose that's needed to get the response. So the open bars are just acetylcholine, so that's providing the baseline.

After that, the animals are exposed to 1.3 part per million acrolein for two hours, and after the acrolein exposure, then they're given acetylcholine one hour, two hours, six hours for twenty-four hours after the acrolein exposure.

So following the acrolein exposure, it takes much less acetylcholine to cause the same doubling of airway resistance. So, therefore, acrolein appears to sensitize the lungs to hyper-respond, and this effect is seen even at 24 hours.

Okay. Now, this graph -- or these graphs are showing what happens when the animals are given either the leukotriene synthesis inhibitors or the leukotriene receptor antagonist just prior to acrolein exposure. The upper and lower graphs are where the leukotriene synthesis inhibitor was given. The middle one is showing the leukotriene receptor antagonist.

So starting from the left, the open bars are the control or the baseline. The animals are just given acetylcholine. The hatch bars, PD, is post-drug. So that's showing given just the leukotriene receptor antagonist or the synthesis inhibitor, there's no effect on the effective dose, the ED 200.

Then acrolein is given to all the animals. acrolein exposure 1.3 part per million for two hours, and then following the exposure, again it's the acetylcholine one hour, two hours, six hours or twenty-four hours after. And it's certainly not the picture we saw on the slide before without the inhibitors or the antagonist.

So, basically, to kind of summarize the results, acrolein exposure produced this transient increase in pulmonary resistance that was reversible after the cessation of exposure. It lasted about an hour.

Acrolein decreased the effective dose of ED 200 of acetylcholine necessary to double specific airway pulmonary resistance in exposed animals, and that effect lasted about 24 hours. The leukotriene receptor antagonist and the leukotriene synthesis inhibitors attenuated the acrolein-induced hyper-responsiveness.

And then the last part of that experiment, the authors measured concentrations of a specific leukotriene, the LTC 4, and they found that it did increase in the broncho-alveolar lavage fluid after acrolein exposure. And when they gave the synthesis inhibitors, they did not see that increase in that leukotriene.

In addition to the broncho-reactivity, acrolein causes mucous hypersecretion. In rats, tracheal mucin, messenger RNA and mucin glycoproteins were elevated in lung tissues following in vivo exposures to 3 part per million acrolein, six hours a day for two weeks.

Similarly in mice, acrolein exposure resulted in significant increases -- in this case, macrophages and neutrophils they found in the fluid, which are indicative of the inflammatory response, along with the increased mucin, messenger RNA synthesis and secretion.

The next slide. Human invitro data, results from two studies are summarized here. The first is also

by Borchers who is from the previous slide. It was reported that invitro acrolein can act directly on airway epithelial cells to increase mucin messenger RNA levels.

In the second study, this is from a different laboratory, Ru et al. 1999. These investigators were looking at the interaction between passive sensitization of human isolated airways and acrolein exposure. They took lung tissue from non-atopic, non-asthmatic patients, and they bathed the tissue in the sera from atopic asthmatic patients, and they reported that the passive sensitization, in addition to acrolein exposure, have a combined effect on the bronchial smooth muscle reactivity in response to different agonists.

In the tissues that were sensitized by incubation, pre-exposure to acrolein for either 10 or 20 minutes, resulted in a significant increase in the maximum contractile response to either a specific or non-specific agonist.

And so, just to summarize, we don't have evidence of a direct effect. We have a large number of studies that indicate that allergic airway diseases, including asthma, are associated with air pollution, of which acrolein is a component.

The Leikauf study, which was the first study,

described studies in the guinea pig of acrolein-induced hyper-responsiveness to acetylcholine and broncho-constriction, which could be considered analogs of response in asthmatic humans exposed to reactive irritants.

Clinical studies, as well as animal studies, have shown that exposure to various air pollutants, particularly reactive irritants, can increase responsiveness to allergens in relation to broncho-reactivity. And formaldehyde is a better studied example of that.

Studied invitro acrolein potentiated the contractile response of immunologically sensitized human bronchial tissue to specific antigen stimulation.

In animals, acrolein exposure causes mucous hypersecretion. And in isolated human cells, acrolein increased mucin messenger RNA levels.

CHAIRMAN FROINES: Thank you. We're going to take a break shortly, but why don't we have some discussion before we take a break?

DR. ATKINSON: So based on what I've seen of the ambient data in L.A., I would suggest that the chronic REL -- or the air concentration divided by the chronic REL for acrolein and formaldehyde are probably pretty similar.

DR. FUCALORO: Would be what?

DR. ATKINSON: Similar.

DR. MARTY: Similar. It's true. It is --

DR. ATKINSON: I don't dispute that acrolein -- if you take the air concentration divided by the REL, acrolein may indeed be higher than formaldehyde, but I would be surprised if it's 200 times.

DR. MARTY: Good point.

DR. FUCALORO: If you reduced the concentration by a factor of 100 as you had previously suggested --

DR. ATKINSON: No. That comes down to two to one. Yeah.

DR. FUCALORO: Yeah.

DR. BYUS: So could you just -- the child sensitivity issue now, I mean it's -- could you just -- where are we?

DR. MARTY: What's the connection?

DR. BYUS: What's the connection? Yes.

DR. MARTY: Okay.

DR. BYUS: Is it just that children are more likely to have asthma?

DR. MARTY: The connection is -- exactly. The discussion we had earlier where we are viewing asthma as the disease that impacts children disproportionately.

DR. BYUS: Okay.

DR. MARTY: And we had evidence here on a biochemical level and in vivo animal studies showing that acrolein is capable of doing of what asthmatic exacerbants can do: Hyper-responsiveness of the airway, increase the mucin secretion.

DR. BYUS: But there's no direct evidence that it does that any more or less or the equivalent in children?

CHAIRMAN FROINES: You won't find any human data. It's because acrolein is so much part of air pollution that you won't find any, you know, unique exposures in a --

MS. POLAKOFF: Well, it's too hard to measure.

CHAIRMAN FROINES: I just -- not that I'm aware of.

DR. BLANC: So comparing head on to formaldehyde and acrolein, acrolein is a more potent irritant. Based on your data, the ratio, the exposures to REL is certainly much higher for formaldehyde and you're discounting --

CHAIRMAN FROINES: Acrolein.

DR. BLANC: And you're discounting acrolein and even discounting your air levels somewhat, which, perhaps, you shouldn't discount because you have data

from the Air Resources Board saying they believe they've underestimated, you would still come out higher than formaldehyde even if you significantly discount it.

So I think the truth has to be somewhere between the data you have and the data they have because that's -- because we know that we're underestimating. We don't believe that that's the same problem as with formaldehyde. The only thing that --

DR. BYUS: The biochemical thing is much better for acrolein. Much better.

DR. BLANC: Well, the data we were presented.

DR. BYUS: Yes. The one we were presented.

DR. BLANC: There is a lot of literature out there on formaldehyde, but it's certainly been better studied in controlled human exposures. But we know that acrolein is much more potent than formaldehyde and is, generally speaking, under-regulated relative to formaldehyde I would say.

So the only thing that's driving you is the Krzyzanowski study, not of asthmatics, but where the peak flow in children -- where they didn't measure acrolein and there probably was co-exposure with acrolein, and the two tend to run parallel also in the kinds of environments they were looking at probably, that you would favor acrolein were it not for your

interpretation of the Krzyzanowski study; is that a fair characterization?

DR. MARTY: Yes. I would add a little bit to that. We were unsure enough about the concentrations in air that even though acrolein scored way high, we were a little bit reluctant to put it in Tier 1. That may have been not a good decision. I don't know.

We also were concerned about the ratio of the ambient data to the REL. And even if you divided by 100, you're still above the REL, and you have about the same ratio of formaldehyde and acrolein.

CHAIRMAN FROINES: Can I ask you a question that goes to Paul's? In terms of -- the guinea pig data is -- it's a nice, solid set of data, and so it's compelling because it's clear and direct, and you can live with it and --

DR. MARTY: And if you're a toxicologist, you like that.

CHAIRMAN FROINES: Toxicologists love that. That's exactly why we do toxicology.

What's the comparable literature? Because since you don't point out any animal literature on formaldehyde, does that mean that the data is by and large negative? Does that mean that there's not data that you think is relevant or what -- clearly people

have been studying formaldehyde much more than acrolein. So what is the circumstances? What are the circumstances?

DR. BLANC: Depends on who they delegated the --

DR. MARTY: That's a good question.

DR. BLANC: -- the literature review to, doesn't it?

DR. MARTY: Well, we --

DR. BLANC: I doubt the literature review was done by the same person, was it?

DR. MARTY: No, they were not. I think what we did with formaldehyde, because we had so many studies, actually, in people, that we did emphasize those. But we can go back and look at to see if there are any of the same sorts of data at the biochemical level for formaldehyde as there are for acrolein.

My guess is probably not because -- because of this issue of people saying, "Well, we don't think it really exacerbates asthma," unless you've had occupationally-induced formaldehyde-specific asthma.

So I don't know if that data are there. They certainly didn't pop up in the search that was done.

DR. ATKINSON: And the other thing you have to be careful about is comparing ambient data from one

decade to a decade differently because the concentrations have been decreasing quite steadily. If you look at formaldehyde in the L.A. Basin, they've gone down by a factor of about ten in the last 20 years or so. Twenty to thirty years.

And it seemed every time they do a field study and do extensive measurements, the concentrations are lower than previously.

DR. FUCALORO: Roger, can you help me on this? Just looking at the formula for acrolein, it looks like it's a type of product that wouldn't last long in the environment. It seems to be pretty --

DR. ATKINSON: It's pretty -- yeah. But formaldehyde has an even shorter lifetime. Formaldehyde photolyses -- well, acrolein my photolyze. We don't know enough about its lifetime.

I mean, the other one is that acrolein can only be formed in the atmosphere from dyeing, such as 1, 3-Butadiene, whereas formaldehyde is formed from almost all organics. In L.A. it's believed that something like 80 percent of the formaldehyde is formed in the atmosphere.

DR. BLANC: I guess my bottom line would be from where I sit with the information that you've given in my role, you know, as a scientific, tertiary

reviewer, that I think the argument is more compelling for acrolein to be in the top five than for formaldehyde to be in the top five.

I guess I wouldn't -- you know, I'm not going to get in the argument about whether or not formaldehyde should have made it from your list of 35 into some shorter list. I don't think it's reasonable given all the questions that you have to have done that step. But I think that prior to your next submission of a revised document, you should think very long and hard about the relative position of those two chemicals.

Now, I think you have a problem in sort of weighting -- given the nature of the exercise that you're going through and the regulatory implications, you're probably -- you've probably made the right choice by not including both aldehydes in the same short list because it would really be sort of really dominating what was driving the five chemicals.

So I think your inclination to choose between the two of them was probably appropriate in taking the global challenge of what you were trying to do. But my own inclination, based on the information you've provided so far, would be that the evidence weighs in favor of acrolein in a relative basis. And that would be driven, I think, by its -- the potency of its

irritancy, the scenarios for exposure, including from combustion products and indoor sources, and its relative under-attention from a regulatory point of view.

And one of the goals of the legislation was to make -- to force the Air Resources Board to take a hard look at a short list of chemicals in ways that could drive control steps. Then this would be one of the ones I would say, "Yeah. Take a hard look at this one."

CHAIRMAN FROINES: I want to make one comment to Tony. The one thing that's interesting from a toxicologic standpoint, chemical structure standpoint of acrolein, is acrolein is, you know, a double bond connected to an aldehyde group, and so that compound undergoes mycliditions (phonetic) with nucleophiles, so it is a very powerful electrophile in that respect.

DR. FUCALORO: That's why I said I didn't expect it to last long in the environment.

CHAIRMAN FROINES: Right. And so therefore, without getting into -- the problem is people have studied the carcinogenicity of formaldehyde pretty extensively. There is a database there. People have not studied the carcinogenicity of acrolein to the degree that one would like. But I would suggest that acrolein is likely to be a carcinogen, and I think over time we'll find that proves out to be the case.

So I tend to agree with Paul in terms of his conclusion because the compound -- although, Roger is right insofar as there are widespread sources of formaldehyde, as we know, and acrolein is more limited in that respect. But toxicologically, I think the argument might favor acrolein. So it's a close call in any way, in any circumstance.

DR. FUCALORO: Of course, there's no unit risk factor given for acrolein. But you said that's because of the --

CHAIRMAN FROINES: Yeah. It's the vacuum, not the negative data. And I think it's worth considering Paul's argument about if we're trying to get ARB's attention with respect to approaching some of these things that haven't gotten attention, then acrolein is a very good candidate for that.

Why don't we take a five- to ten-minute break, and then we'll -- sorry, Melanie.

DR. MARTY: Can I just make one quick comment? There are data looking at formaldehyde and already 50 studies, for example, and in guinea pig models of hyper-responsiveness. It may be worthwhile to flesh that out more in the document and bring it to the panel.

CHAIRMAN FROINES: Well, in this case, I think it's important to try and -- since we're obviously

probably going to argue in favor of one versus the other, the way -- at least the way the discussion has gone, it's good to have some sort of comparability in the information we have to work with.

DR. ATKINSON: I mean, the funny one is that the same database has crotin aldehyde, which is the next log up, ten times higher than acrolein.

CHAIRMAN FROINES: See, if I express my bias, it would be that we have PAHs; right? Nobody worries a bit about PAHs. I would argue that we should have aldehydes and have acetaldehyde, formaldehyde, crotin aldehyde, glutaraldehyde, acrolein and probably a couple others, and it would make perfect sense, but we probably won't do that. But if you're arguing by analogy, we should.

DR. MARTY: If it makes you feel better, I think in terms of engineering controls on combustion sources to reduce one aldehyde -- and Roger can correct me if my assumption is wrong -- you would be reducing most of the aldehydes.

DR. ATKINSON: Yeah, yeah.

CHAIRMAN FROINES: And that is the precise argument that a former ARB staff person made when I complained about doing benzopyrene years ago. She said, "If we do benzopyrene, we'll control all the PAHs." And

what was the comment you made earlier about which compounds have not had control strategies developed? PAHs. So that the notion of doing benzopyrene and PAHs hasn't driven the process, so that obviously we need a different hook. Thanks.

We'll take a break.

(Recess.)

CHAIRMAN FROINES: We have this room until 5:00, so we're going to --

DR. GLANTZ: Talk really fast.

CHAIRMAN FROINES: -- talk really fast and cover all eight of the rest of the compounds. And the -- I think -- is Jim Behrmann here someplace? My guess is that we're going to finish going through these compounds at the May 14th meeting so that I think that's the next phase of this.

In talking with Melanie and George at the break, we talked about what are people's energy levels up to, and I think that we talked about doing lead and, perhaps, mercury in the next hour because, presumably, they are enormous amounts of data, but they're relatively straightforward at some levels as well.

DR. GLANTZ: Can I just ask one question?

CHAIRMAN FROINES: Sure.

DR. GLANTZ: I have to get Melanie's attention.

Melanie. Yoo-hoo.

DR. MARTY: I'm sorry.

DR. GLANTZ: It's okay. When we come back on May 14th, are you going to have done anything to this document or proposed shuffling lists around or any of the -- we had our extremely long discussion this morning about, you know, why -- coming up with sort of why you did what you did and all of that. Are you going to have any of that for us to look at by the next meeting? It would be nice.

DR. MARTY: We'll try to have some of them. We'll try to have the things that you asked us to do in the introduction done.

DR. GLANTZ: Okay.

DR. MARTY: In terms of adding either additional summaries that -- for example, for chemicals that Paul mentioned that are important --

DR. GLANTZ: Yeah.

DR. MARTY: I'm not sure that we can have that done. I realize that gives us one week to do things because you folks need to get the document with some time to look at it.

DR. GLANTZ: Okay. The one thing -- I think that would be very helpful. And, I mean, one other -- if, as a result of the discussions today you wanted to

propose shuffling things around on any of these lists, I think if you were to do that before then, I would -- feel free to do it, you know. If not, that's okay too.

But, you know, just in the interest of -- well, no. In the interest of moving things along. I think that there have been -- as a result of the discussion this morning and some of the things that were said today, you know, you might want to come back to us with some changes in the priorities, and the sooner we get to see those, the better I think. If not, we'll probably get to meet a couple more times about this before July.

CHAIRMAN FROINES: My guess is that to ask them to do much changing and improving of the document is probably not feasible given they have a week but -- so I would focus on trying to make, you know, the best presentation of the remaining chemicals so that the issues are as succinct as possible to help facilitate the process rather than trying to --

DR. GLANTZ: Okay.

CHAIRMAN FROINES: Scurry around and writing, doing a --

DR. GLANTZ: Yeah. That's probably true. But I think, like, one of the things, though, from this morning was the idea that the Tier 2 might get to be a bit longer list, so I think if that were the case, it

would be nice to at least get presentations on the things that you thought ought to be on the -- any additional compounds on the Tier 2 list. You know, based on what was discussed this morning. We might not, you know?

CHAIRMAN FROINES: My guess is --

DR. GLANTZ: Well, why don't you go on?

CHAIRMAN FROINES: -- that we'll be -- there will be 11. We need to get through this by the end of May 14th. Not necessarily make every decision by May 14th, but hopefully make our decisions by May 14th.

DR. GLANTZ: Well, that's true. But that's why I suggest that if the result is that some compounds are going to be added into the Tier 2 list based on the discussion this morning, that we should have some kind of presentations about that.

CHAIRMAN FROINES: I have one question. Is George -- there's George. Sort of a policy level question. George, let's go -- let's assume that May 14th we go through -- get through all the 11 compounds, and the panel continues to have suggestions about changes in the document. The first question, I guess, is when do you need to have a document that goes to ARB for its consideration on July 1st?

And the second question is, Can you go into --

can you give the ARB a list of the five and take some time to develop the document so that the underpinnings for the decision actually doesn't necessarily get there by July 1st, but you can get them a more complete document, say, August 1st or something? I mean, in other words, I'm trying to figure out because there's -- obviously, we're under a very tight time constraint, and the question I'm really asking is, How are we going to deal with the constraints?

DR. ALEXEEFF: Well, the way the statute reads is it's actually the OEHHA director that has to make the decision by the end of June -- I think it's by July 1st he has to identify the top five chemicals.

Okay. Now, we have to do that in consultation with the Air Resources Board. Now, we've already been consulting with the Air Resources Board. So the Air Resources Board does not have to make a decision in this process. We're planning, once we're done with this, to make a presentation to the Air Resources Board because then they have to look at their responsibilities under the act.

So -- but we -- we thought it would be great if we could have wrapped the whole thing up by July 1st, but based upon the issues that you raised I don't -- wrap the whole thing up meaning make a presentation to

the Air Resources Board as well, but that was our original intention.

It doesn't look like it's going to happen based upon the timing. But it's not required to happen by law. What's required to happen is we have to come up with the list of five by July 1st.

CHAIRMAN FROINES: And the -- and the supporting document there's no time restriction.

MR. ALEXEEFF: I don't think there's a requirement for a supporting document, but the basis has to be reviewed -- let me just pull that statute up. The basis has to be reviewed by the Scientific Review Panel and then -- okay. So by July 1st of this year, "The office, in consultation with the State Board, shall establish a list of up to five TACs"; okay? "that may cause infants and children to be especially susceptible to illness." So that's by July 1st.

Okay. Then it says, "The office shall submit a report containing the list and its reasons for including the toxic air contaminants on the list to the SRP." And then the SRP -- so we, quote, have "done that"; right? Then it says, "The SRP, in a manner consistent with" the other stuff that you do "shall review the list of TACs submitted by the office, and as part of the review, any person can submit other information to the panel." You

know, public comment type of period. So that's basically the way the process is laid out.

So I think that the basis for the five should be all crystal clear, if there's five, by July 1st and that we have to list them by July 1st. Whether or not the report is published and finalized is probably not supercritical, but the closer it is, I think -- I think we would probably plan on doing it by -- have it all done by July 1st. That would be our -- we would probably move everything -- all the mountains we could to get it done by then.

DR. MARTY: We have to because I'm going on vacation July 2nd.

DR. FUCALORO: You were going on vacation.

DR. GLANTZ: And she's never coming back.

CHAIRMAN FROINES: Let's go ahead. I think that's clear. I think it puts a lot of -- it will put a lot of emphasis on our really moving the process along on May 14th so we bring it to closure from our standpoint, because we'll want to write some level of findings for ourselves as well.

DR. MARTY: There's another meeting planned in June, yes? Peter.

MR. ALEXEEFF: It would probably be useful to have a meeting planned in June.

CHAIRMAN FROINES: That's fine. This panel decided to have a meeting every two months not long ago. And, of course, we follow it up by planning three meetings in two months. So we're doing very well.

DR. FUCALORO: Why don't we all get jobs at the same university.

DR. COLLINS: You're the dean.

DR. FUCALORO: Former dean.

DR. GLANTZ: Well, most of us do have jobs at the same university.

CHAIRMAN FROINES: Well, I would be quite happy if the governor gave us a bunch of FTEs at you UCLA and we had everybody move to Los Angeles. I'm not sure Roger and Craig and Stan would buy into it, though. I've been trying to get Paul to do it for years.

DR. BLANC: We should start. Really we need to start.

CHAIRMAN FROINES: Melanie.

DR. MARTY: The next chemical we're going to talk about is lead, and I just want to preface it by saying this panel has looked at lead as a TAC not all that long ago. The information focused on developmental neurotoxicity and effects in children. We didn't think we needed to review in detail that information again today, so we have a pretty brief presentation.

DR. WINDER: So lead was selected for Tier 1 for these reasons: It's well documented to have very extensive neurotoxic and developmental effects. And these neurotoxic effects are more pronounced during exposure in early childhood. There is some evidence for prenatal exposures as well.

And low level exposures, in this case the literature talks about 20 or 30 micrograms per deciliter in the blood, are associated with developmental delays, decrements in intelligence, memory, visual motor function, perception integration and behavior.

Now, no known data so far support a distinct threshold for effect. And the other reason for considering lead in child-specific behaviors seem to be -- involve making kids more at risk. Also, just child-specific physiology, for example, the absorption of lead is much more rapid in kids two years and younger.

So we're summarizing, as Melanie was saying, the major studies that were involved in this. Up here we show the coefficients which were associated with the effects of lead on intelligence using the WISC-R intelligence scale, the revised version. And these are broken down both into crude models and adjusted models, as well as meat-analyses.

In all cases, we've shown the coefficients of the correlation here in the right-hand column, and, in general, you'll see a familiar correlation between the levels in blood and performance levels on these intelligence tests, and this seems to hold throughout all these analyses.

Then this next table, this is something that OEHHA worked up to try and examine what would happen at certain blood lead levels. Now, we show on the left-hand column our average air lead concentrations in micrograms per cubic liter. The top one being the -- roughly the current level in California for the ambient lead.

And then the next column over where it shows the geometric mean of 3.14, this is from NHANES. This is the, at that time, average across the United States. And then each of the subsequent columns are kind of what if kind of situations. If we reduce the lead in the blood or if we change the geometric standard deviation, how many children does this push above that magic number of 10 micrograms per deciliter of blood lead? And so as you see here, with the -- in a minor decrease in the geometric mean where you see substantial decreases in the percentage of children which will actually end up in that above 10 micrograms per deciliter.

And as we approach the bottom of the graph here, the 1.5 micrograms per cubic meter, our current regulatory level, as much as 45 -- 46 percent of the kids will move into this above 10 microgram per deciliter level.

CHAIRMAN FROINES: I just have one question. Is the -- what is -- you have two GSDs say at the top of the row, and what's the basis for those? Are they from NHANES calculations? Are they -- one is for one year olds and the other is for two year olds? I don't quite understand that table.

DR. MARTY: Yes, that's exactly right. The -- the geometric mean of 2.1 represents kids who are ages 1 and 2. And I think the other geometric mean is older kids.

DR. FUCALORO: And the number you cited, the .055, the document says that the California 1999 was actually lower than that, 0.014, according to the document.

DR. MARTY: Um-hmm.

DR. FUCALORO: It's a quarter of what's there.

CHAIRMAN FROINES: .014?

DR. FUCALORO: .014.

CHAIRMAN FROINES: Or .14?

DR. FUCALORO: .014. Unless it's an error.

That's always a possibility.

DR. MARTY: What page?

DR. FUCALORO: Look on page 2. Unless I'm reading it wrong.

DR. MARTY: I know it's lower than the .05 but I can't -- oh. Okay. According to CARB's monitoring network, they are saying the ambient air lead concentration in California in '99 -- that would be a mean -- was .014.

I think the point is that there -- existing blood lead levels in children, there is a concern adding more lead into the air of pushing more kids above the level of concern as identified by the CDC of 10 micrograms per deciliter. That's really the point of this.

DR. FUCALORO: Yeah. I think that's the thing that's a little confusing in the sense of reading it that the ambient air concentration does not seem to explain the level of lead in the blood. So one can infer from that, one may infer from, that they're getting lead into their system in other ways. Ingestion or --

DR. MARTY: There's no argument that they're getting lead from lead paint ingestion --

DR. FUCALORO: Yeah.

DR. MARTY: -- and other sources.

DR. FUCALORO: Right.

DR. MARTY: There's no argument there. If

DR. FUCALORO: Soil, picking it up.

DR. MARTY: Right. What we're concerned about is twofold. Additional lead sources emitting into the air. It's not -- as you now, as you can see from this information, lead exposure is on a regional basis, which is what the air monitoring network gets at are probably not much of an issue. We are concerned with hot spots of exposure.

DR. FUCALORO: An average is only an average. I mean, the distribution of values is the most important. I understand.

DR. WINDER: Okay. So next slide, please. Looking at some of the more recent data to address the question of whether or not negative effects associated with blood lead levels below the 10 micrograms per deciliter occur.

These are a couple of studies. In the top one, it's a little bit complicated to explain here, but in the top one, Campagne et al., we're looking at both the mother and cord blood activities of calmodulin-stimulated calcium pump activity. So what we're looking at here is measuring lead levels in mother's hair, in

cord blood and in the newborn's hair.

What we see over here in the left-hand side, they did this experiment looking at both the calcium pump activity unstimulated with calmodulin and then the bottom two rows were stimulated with calmodulin to see if there's an effect of the stimulatory property and broke it down into the level at less than .7, and this is looking at the lead in the newborn's hair, .701, .5 and greater than 1.5.

And what we see here is that, according to this series of studies, if you look at the cord level unstimulated with calmodulin and as stimulated with calmodulin, we find that there's a pretty significant decrease in the calcium pump activity associated with increases in the lead.

Now, the second graph in the bottom is trying to give you a handle on -- since the top graph is looking at lead in infant hair, in the mother's hair, the bottom one is giving you a feel as to what that corresponds to in blood lead. So, for example, in the cord blood on the right-hand column in the bottom graph, the cord blood was showing the lead at 4.8 micrograms per deciliter, and that corresponded to 1.1 micrograms per gram of lead in the newborn's hair.

And so you see this level of 1.1 is right in

that middle set up there in the top column. So what this is showing is that the effects that we're seeing, in this case the inhibition of the calcium pump, are happening at blood levels well below the 10 micrograms per deciliter level. Roughly half. So this is suggestive evidence that the -- that 10 micrograms per deciliter may be too high.

Now, there's an additional study which was looking at the -- unfortunately, we don't have a slide on this one. A gentleman was looking at the brain stem, auditory and vocal response, which is commonly used in a lot of these neurotoxicology studies.

And, again, he was finding that in children with blood lead levels below the 10 micrograms per deciliter, that is, from zero to seven and seven micrograms per deciliter up, they were seeing effects on -- let's say they evoked a response. That is to say, increasing lead increased the conduction interval associated with this DRE.

As the blood lead levels rose higher, the conduction interval got shorter. We don't know why that is. The authors are speaking that lead is, in fact, at low levels inhibiting the growth of the neurites. And at other levels in addition to that may be affecting the myelination.

The upshot that the researcher gives is that these levels -- these effects are being seen at less than the 10 micrograms per deciliter.

DR. MARTY: I think part of our point is that we are currently treating non-cancer health effects of lead and no threshold phenomonon, at least at concentrations that we can observe in our modern environment. And there continues to be information that you can see effects, at least at the biochemical level and at the cellular level at concentrations below 10 micrograms per deciliter.

CHAIRMAN FROINES: Do you have any idea what the concentration of lead in the air in Los Angeles is? Because the .014 is a California-wide. It's clearly going to be different in an urban environment.

DR. MARTY: We can look that up.

Jim, do you happen to know by any chance?

DR. FUCALORO: While they're looking it up, very often my place has students study the soil. There's a lot of lead in the soil. It's still there. Not surprisingly I guess.

CHAIRMAN FROINES: Well, they still use leaded oil, leaded fuel in airplanes.

DR. MARTY: We were looking at some of the information from the Air Toxics Hot Spots Risk

Assessments that we received from the facilities emitting lead into the air. In a couple cases, we did get one hour maximum modeled concentrations that were considerably above the existing standard ambient air quality standard, which is a hard comparison to make because that's a 30-day average in time.

One of them was about 5 micrograms per cubic meter. There was an earlier risk assessment that we saw way back in 1990 where they had model concentrations as high as 50 micrograms per cubic meter for a one hour max. So we are --

CHAIRMAN FROINES: But those are out of secondary smelters I bet, aren't they?

DR. COLLINS: This was a battery company.

DR. MARTY: Battery.

CHAIRMAN FROINES: Secondary smelter, battery company.

DR. MARTY: Right. Right. So we still have a concern about hot spot exposures. And, in addition, we have a concern about the no threshold phenomenon and adding additional lead burden to the -- to kids particularly.

CHAIRMAN FROINES: Well, I think that if you look at the airborne concentrations of lead in the L.A. Basin you would probably -- and then run it through the

various models, whichever ones you choose, you'll find a fair percentage of kids predicted to have blood leads over ten.

DR. MARTY: That also goes by race and ethnicity. African-American kids have higher blood levels from --

DR. FUCALORO: Environment.

DR. MARTY: Right. Right. So they, as a population, are a sub population of kids who are particularly at risk.

CHAIRMAN FROINES: Comments? Questions?

Mercury.

DR. GLANTZ: I guess I have one quick comment. I think in terms of the placement as one of the five, lead is pretty uncontroversial.

CHAIRMAN FROINES: It would have a high ridicule value not to show up on the list.

DR. GLANTZ: Yeah.

DR. WINDER: Okay. So in talking about mercury, mercury was put on Tier 2 as opposed to Tier 1. The reason for considering it on List 2, again, it's a neurotoxicant with a fairly well-defined series of symptoms. Again these manifest themselves primarily in young children.

A lot of the studies that you find published

deal with methylmercury exposure both in utero and postnatally, and these effects are seen at levels that are far below those especially for adults.

The reason for considering it Tier 2 as opposed to Tier 1, is that in California at least, air is a relatively minor transport medium for mercury.

Now, next supplied, please. The evidence for this differential effect in children versus adults. Much of this again derives from methylmercury data on children. In this case, we're looking at Minamata, a disease in Japan. Where children were displaying this -- this I'll describe as congenital cerebral palsy, and their lead -- I mean, their mercury concentration hair was, as you see the range here, 5.22 to 110 parts per million.

Now, in that same group, the mothers were examined, and their maternal hair, as you see below that, is over a somewhat broader range and generally a little bit higher. The significant thing here is that the children were expressing fairly severe symptoms. These included mental retardation, ataxia, limb deformities and may cases -- or in some cases death.

Whereas for the mothers, their symptoms were usually paresthesia, fairly mild tremors, limb pains, this kind of stuff. So -- and there are a number of

other reports, not just from Japan but elsewhere. For example, the Iraqi studies, which suggest that, again, very often mothers who present as having few or no symptoms and yet have severely affected children.

Now, as with lead, again, the same kind of concerns about children's behavior being one of the things that figures into this higher exposure.

Now, the next slide, please. In this study, this is by Marsh et al. This is looking at the mothers and children -- mother and children pairs in Iraq that were exposed to lead treated -- excuse me, mercury-treated grain. And in this particular instance, what we're looking at is the -- the kids were examined in several different categories, looking at motor effects, looking at the effects of mercury in speech, mental performance and frequency of seizures.

Now, this particular graph is broken up into the mercury levels seen in the mother's hair. Now, what this shows, in all cases, the dark blue bar is significantly higher than the rest, showing that at the higher levels of mercury in the mom's hair, 99 to 384 parts per million, there is substantially greater representation of the children with these motor defects, deficits in speech, performance in mental tests and frequencies of seizures. And the significance levels of

these things are at the .01, .001 levels.

DR. BLANC: I think you can probably go fairly rapidly through the slides on the pediatric sensitivity to mercury. I don't think there are going to be any -- so all of it's going to revolve around how you approached the potential for airborne exposure and how small, theoretically, an incremental exposure would have to be for something for which you would imagine that the bulk of the exposure is perhaps through diet, but whether or not you think any increment would be relevant or what -- how small an increment it would have to be to be relevant.

DR. MARTY: Let's move to the exposure slides then. Is that okay with you, Bruce? Or do you have slides that are relevant to the question?

DR. WINDER: Well, these are again slides that look at the effects associated with mercury.

DR. MARTY: Okay. I think we've established that kids are more sensitive to it than adults. The reason we ended up putting it on Tier 2 is because of what we talked about earlier, that airborne exposures, at least on a regional basis, don't appear to be contributing a lot to total mercury intake.

We did come up with some information from --

DR. WINDER: This is from -- the presentation

is on the screen right now. This is some data from a very recent meeting in San Francisco sponsored by EPA. They're looking at mercury emissions from various mine sites around the state. These typically are mines that are no longer active. They were once involved in gold mining, in some cases. Subsequently, mercury mines.

So what you see here is this sulphur bank mine, for example. They show a flux of mercury of 922 nanograms per miter squared per hour. In that particular mine situation, the authors calculate based on the actual exposed surface area that there's an annual flux of about 6.5 kilograms per year of mercury into the air.

Down into the McLaughlin Gold Mine, this is broken up into two areas, the pit, which is the actual mining area is, as you see, putting out some 674 nanograms per meter squared per hour. Whereas the mine tailings, which include mercury associated with extraction of the gold, putting out somewhat higher than 1,000 nanograms per meter squared per hour.

So this gives a calculated flux for the -- both areas around 15 kilograms per year, which comes out to around 32 pounds per year. Now, that's substantially higher than what the ARB tells us lead emissions by facility are. Those -- particularly for the state.

Excuse me mercury emissions by the facility, particularly for the state, are limited to around 6 pounds.

So there are some, as Melanie put it, some hot spots of mercury vapor throughout California.

DR. MARTY: It would be nice if we had a nice model like the IEUBK model, which relates blood air concentrations to -- blood lead concentrations to air lead concentrations. We don't have a similar model for mercury.

Nonetheless, the concentrations measured in air are around -- in the nanogram per cubic meter amounts regionally. Bruce has an example where it would certainly be higher than that judging by the emissions rates that you see on the screen.

So, again, it's not a regional problem, may be a hot spots problem, but the concentrations still are relatively low.

DR. BLANC: Do you have a -- a main priority cutoff for how many hot spots there need to be for something to raise up in your prioritization based on hot spots once you know that the ambient levels are not the issue?

DR. MARTY: We don't.

DR. BLANC: Is -- would ten be too many? Are

five too few?

DR. MARTY: We actually didn't discuss that.

DR. BLANC: And do you have --

DR. MARTY: In terms of lead, there's probably around five.

DR. BLANC: So that was enough for you for that?

DR. MARTY: For mercury, you do get mercury emissions from, for example, municipal and hospital waste combustion processes since it's not trapped.

DR. BLANC: That's what I wanted to ask about specifically. So do you have a level monitoring data that tell you what the emissions are near hot spots that have medical waste incineration?

DR. MARTY: We don't have monitoring data. There are some modeling studies that have been done looking at mercury from medical waste incinerators primarily. We can look at some of that.

DR. BLANC: Does your document list how many medical waste -- licensed medical waste incinerators there are in the State of California?

DR. MARTY: No. No.

DR. BLANC: Wouldn't that be something you would want?

DR. MARTY: Yes. There's far fewer than there

used to be because the dioxin airborne toxic control measure really forced people to stop burning medical waste onsite and instead transport it to a state-of-the-art regional facility.

DR. BLANC: But mercury is not captured in those; right?

DR. MARTY: No, it's not.

DR. BLANC: So basically what you've done is tightened the concentration at the hot spots but limited the number of hot spots.

And do you have any ambient airborne monitoring data from Santa Clara County in the areas near the former Almaden mining operations?

DR. WINDER: No, I don't.

DR. BLANC: And have you contacted Santa Clara County health officer to see if they have some control over data that you might not be able earn?

DR. MARTY: No, we haven't done that. We should do that.

DR. BLANC: That's the largest mercury mine in the world formerly. I think it would be worth it.

DR. MARTY: I think it definitely would be worth looking at.

DR. BLANC: Again, it's kind of the parallel to your argument on lead. But since you're going to put in

the top five, I think you're not going to get any argument from us here. And, clearly, mercury is, in your group, getting very close consideration, and you're not going to get any argument about that either.

The question is, Have you met enough of a burden of disproof? Have you proved the negative enough to satisfy yourself that it shouldn't be among the five or at least it's outweighed by the things that you have chosen? And, you know, I think that's going to be something that we're going to have to look at closely.

DR. MARTY: We'll have to be -- to bolster that explanation --

DR. BLANC: Yes.

DR. MARTY: -- in this document.

DR. BLANC: Because I'd hate to have us miss the boat on that just because we didn't ask the right questions.

DR. MARTY: Right.

DR. BLANC: And, you know, again, it's all relative, but if we're looking at the -- and we're not going to go into the other four things. What table is the final one? I'm sorry.

DR. MARTY: It's Table 1, page 8.

DR. BLANC: What page is it on?

DR. GLANTZ: We may have time to get one or two

more.

DR. MARTY: Page 8.

DR. FUCALORO: Dioxins.

DR. BLANC: Yeah. But let's say we're looking at dioxins and PCBs; right? Now, you've said -- you've just said that, for example, for medical waste, the dioxins at least are being destroyed by the temperature pheresis.

DR. MARTY: Not entirely. But yes, the idea was to reduce the emissions.

DR. BLANC: Whereas we know that mercury is not being touched.

DR. MARTY: Yes

DR. BLANC: And is not being captured. So in terms of this, you know -- and with dioxins, we're really not talking about ambient concentrations either, I don't suppose. We're talking about hot spots also; aren't we?

DR. MARTY: It's both. It's regional exposures and hot spots for dioxin.

DR. BLANC: Well, maybe those are the two. We were sort of inherently pairing lead and mercury in this discussion, but maybe the discussion is more parallel for dioxins and for mercury.

CHAIRMAN FROINES: Do you know, by the way, if

there are any mercury thermometer plants in California?

DR. MARTY: I don't know. I don't know. That we can ask ARB. We can try to figure out how many facilities there are emitting mercury also in the hot spots database. You just add them up and where they are.

I think it's fair to point out, though, that the, quote, "mercury problem in California" is because we mined it in the foothills, we dredged it -- trucked it across the valley and used it for gold mining in the Sierras, so we contaminated a lot of streams, and it's since run down and just spread itself all over the foothills and the valley, contaminating food sources for people. So that's a pretty important exposure for mercury.

DR. BLANC: I know it's an incremental issue you're dealing with.

DR. MARTY: Yes.

DR. BLANC: But your statute clearly tells you that you need to take that into account, and it doesn't really matter whether the air source is the bail of hay or it's the straw that's breaking the camel's back. Either way, you need to deal with that, and that makes your life pretty complicated.

But still, for this one, it's proving the

negative argument I think that's going to be critical and not simply saying -- since you already have disproved the validity of the -- in the release inventory; right? Your slide on the mines, those mines are in California?

DR. WINDER: Yes.

DR. BLANC: So you already know that there's far more mercury going up than the release inventory tells you is going up; right?

DR. WINDER: Yes. I mean, our inventory for the state was something like 6,400 pounds or thereabouts per year. And as you see from this for example, McLaughlin, it was about 33 pounds per year. So it's a small portion of that, but your point is well taken with regard to the slides.

DR. FUCALORO: It would helpful -- I asked Paul this. Would it be helpful to play mercury off against lead? They both seem to have the same sorts of things. They're both extremely toxic, and their exposure level is low now and probably getting lower. And one of them is going to make the first tier and the other is going to make the second tier. So would a comparison between those two be useful?

Paul, I asked you that question.

DR. BLANC: What I was saying was maybe not.

Maybe the comparison should be between dioxin and mercury.

DR. FUCALORO: You're thinking dioxin. Sorry.

DR. BLANC: Well, you can say that it's the obvious one, but maybe it's not so obvious.

DR. MARTY: Yeah. And the natural inclination is to look at the two metals that are developmental neurotoxins in humans. Well documented.

DR. BLANC: But the real issue is that you have two substances in the group -- in the top group, both of which everybody is going to say is not of the big player. They both made it into the top 11 one way or the other. That's dioxin and mercury. But they're the one for which the air exposure data are the lowest of all these but they both --

DR. MARTY: I think maybe a little bit of -- in the case of dioxin, almost all the dioxin that ends up in the food chain initially was airborne from combustion sources. Bleaching of pulp during paper making used to be a significant source and is responsible for a lot of the residual that you see near pulp mills. But, currently, the dioxin that enters the food chain came out of some combustion process somewhere.

You can't really -- so we viewed it as, okay, the problem is controlling it from coming out in the

first place. In the case of mercury, it's really -- it's a little bit different in that the primary sources are water born, not initially airborne. So that's one thing that we weighed when we looked at aggregate exposures.

DR. BLANC: Except that you have no way of controlling the dioxins probably.

DR. MARTY: It's sure getting a lot of attention at U.S. EPA and also at CPAAPCO, the California Association of Air Pollution Control Officers have a project they're doing, trying to figure out if residential burning in California, and that's, you know, burn barrels is a significant source of dioxin. So they are trying to focus a little more on where the dioxin is coming from.

There's a lot of papers on global flux of dioxin, and it seems that there's more that you can measure out there than you can account for in terms of emissions. So it's -- which is -- it's a tricky thing to do but --

DR. FUCALORO: Naturally occurring.

DR. MARTY: Lots of people are looking for where is it all coming from? And also I should add that ARB did look at our list and didn't flinch at -- when they saw that dioxins was in the top tier. You know,

some of the comment we got from them indicated that they thought they could do more to control dioxin.

CHAIRMAN FROINES: I think that that's a -- Paul's also raising a generic issue within the context of the specific one, which is when we get down to the final five, I think we'll need -- we want to have a clear discussion as to how the ultimate selections were made relative to each other.

And this points out -- the issue of dioxins versus lead versus mercury points out that you have on the one hand the strength of the evidence, and the second is, of course, the exposure, and those two will probably be the defining features. But, in general, we'll have to make sure that those are well described.

My guess is that this is a good time to stop for the day. I don't think we should take up another chemical.

DR. FUCALORO: Good guess.

DR. BLANC: Yeah. Good.

CHAIRMAN FROINES: Can we have a motion to adjourn?

DR. GLANTZ: So moved.

DR. BLANC: Second.

CHAIRMAN FROINES: All in favor?

ALL: Aye.

CHAIRMAN FROINES: The meeting is officially closed for April 27th, 2001, with the Chair's thanks to everybody who participated.

(Proceedings concluded at 4:40 p.m.)

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STATE OF CALIFORNIA

I, Jennifer S. Barron, CSR 10992, a Certified Shorthand Reporter in and for the State of California, do hereby certify:

That the foregoing proceedings were taken down by me in shorthand at the time and place named therein and were thereafter transcribed under my supervision; that this transcript contains a full, true and correct record of the proceedings which took place at the time and place set forth in the caption hereto.

I further certify that I have no interest in the event of this action.

EXECUTED this_____day of_____, 2001.

_____

Jennifer S. Barron, CSR #10992