MEETING

STATE OF CALIFORNIA

AIR RESOURCES BOARD

SCIENTIFIC REVIEW PANEL

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

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PANEL MEMBERS

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Paul D. Blanc, M.D.

Alan R. Buckpitt, Ph.D.

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Beate Ritz, M.D., Ph.D.

REPRESENTING THE AIR RESOURCES BOARD:

Mr. Peter Mathews, SRP Support Administration

REPRESENTING THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT:

Dr. Andrew Salmon, Chief, Air Toxicology and Risk Assessment Unit

Dr. Joseph P. Brown, Ph.D.

Dr. Melanie Marty, Deputy Director, Scientific Affairs

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PROCEEDINGS

CHAIRPERSON FROINES: We will call the meeting of the Scientific Review Panel to go forward at this point. And we'll be getting some more paperwork. But I think we're in pretty good shape.

I want to introduce two people. One, you've presumably met before over the phone, and that's Gina Solomon, who is the Deputy Secretary of Cal/EPA. And I offered to let her speak in whatever way she wanted and she just said, "I'll pass."

The second person is a new member of our Committee, who perhaps many of you know, but it's Dr. Beate Ritz, who is the Chair of the Department of Epidemiology at UCLA School of Public Health. So Beate is our new epidemiologist for this Committee.

So Mark? Melanie?

And I want to remind people that we generally are letting the OEHHA people give their presentations without -- unless it's absolutely necessary to ask a question for clarification, and then we have the discussion following that. So try to keep questions to a minimum.

PANEL MEMBER HAMMOND: Something that was just passed out that doesn't have a name on it. I would like to know who it's from.

PANEL MEMBER BUCKPITT: I shall remain nameless.

PANEL MEMBER HAMMOND: Thank you.

CHAIRPERSON FROINES: We'll come to him.

PANEL MEMBER HAMMOND: I just wanted to know.

CHAIRPERSON FROINES: Just for those who don't know, Alan Buckpitt is the lead on butadiene. So we'll be hearing from him in the near future.

Melanie.

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: Melanie Marty from OEHHA. So I just wanted to actually transition -- give the Panel an idea of what's happened at OEHHA in the recent past and transition my role over to the person who is now doing it.

So when Dr. Alexeeff was approved as our Director, he made some changes reorganizing the department. And I'm not the Branch Chief for the Air Branch anymore. Instead, Dave Siegle is. Dave.

CHAIRPERSON FROINES: Welcome.

AIR BRANCH CHIEF SIEGLE: Thank you.

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: So you guys will not be hearing from me much, and you will be hearing instead from Dave and still Andy.

CHAIRPERSON FROINES: How long have you been in that position?

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: Since June.

PANEL MEMBER BLANC: In the former position.

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: Oh, my gosh. Fourteen or 15 years. Fourteen or 15 years. I can't remember now.

CHAIRPERSON FROINES: Well, thank you. It's been a wonderful experience for us to work with you.

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: Thanks. I appreciate it. And likewise. This is actually a fun thing to do because you learn so much at these meetings.

PANEL MEMBER BLANC: What are you going to do now?

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: Currently, I'm Assistant Deputy Director for Scientific Affairs. So nice bureaucratic name. Look at that and say, "What is that?" I'm helping George and Lauren at least run the department on the science side, so the science programs.

PANEL MEMBER BLANC: And how does that interface with, let's say, your successor here? What are the -- I know the reporting lines in the AA unit, but would he then get input from you?

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: Yes. I'm working with Lauren Zeise. Lauren is actually the Deputy Director for Science. Lauren is Dave's boss.

That's the line. And --

CHAIRPERSON FROINES: So Paul's question is very relevant. When I want to send you an e-mail, I just send an e-mail or call you. Who do I do that to now?

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: Dave.

CHAIRPERSON FROINES: Dave, okay.

PANEL MEMBER BLANC: And you'll be sending us all an introductory e-mail?

AIR BRANCH CHIEF SIEGLE: I will.

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: And interestingly enough, Dave, when he first came on board and we were the Department of Health Services back then, he was working in the Toxic Air Contaminant Program. So he presented the dioxin document to this Panel in 1985. So --

CHAIRPERSON FROINES: That was in Monterey.

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: What goes around comes around.

CHAIRPERSON FROINES: That was in Monterey. Those were the good ol' days when we could go places, like Monterey.

AIR BRANCH CHIEF SIEGLE: I remember the Queen Mary.

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY:

Thanks very much.

CHAIRPERSON FROINES: And thank you again.

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: Here's Dave.

You are welcome. My pleasure.

CHAIRPERSON FROINES: Since we have a big project on predictive toxicology going on at UCLA, are you the person I call now?

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: Yes, I am.

CHAIRPERSON FROINES: So I can still keep the nasty phone calls going?

AIR BRANCH CHIEF SIEGLE: Any nasty phone calls, Melanie.

CHAIRPERSON FROINES: I don't think you need to worry about that. Okay, Dave.

AIR BRANCH CHIEF SIEGLE: Okay. Well, I'm not quite sure how this goes. It's been a long time. But I'd like to introduce Dr. Joseph Brown, who is going to discuss the reference exposure level for 1,3-butadiene.

(Thereupon an overhead presentation was presented as follows.)

DR. BROWN: Thank you. Well, this is sort of a standard start to our presentation. So you might consider this our boilerplate. For those of you that have been

with us a while, you can recognize that this is our basic authority for what we're doing on RELS. And it falls under the Air Toxics Hot Spots Programs and also the Children's Environmental Health Protection Act, also known as SB 25.

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DR. BROWN: Butadiene is a major commodity product of the petroleum industry. Workers acutely exposed to butadiene experience irritation of the eyes, nasal passages, throat and lungs. Some workers have experienced coughing, fatigue, and drowsiness. Inhalation of butadiene is mildly narcotic at low concentrations and exposure to very high concentrations can result in narcosis, respiratory paralysis, and death. Repeated exposures can damage human sperm cells and increase ovarian atrophy in mice.

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DR. BROWN: I hope you can see this.

This is some environmental occurrence data taken from the Bay Area. This is the most recent data we could get from 2008. You can see the values are pretty low compared to the volumes we'll be talking about today in our RELS. For example, the chronic REL. These values are a couple of orders of magnitude lower. If you pick the highest value there for San Jose, the peak value at .26 is

about 4 percent of the cREL we're proposing. And the average value is less than one percent.

So unlike nickle, which I talked about here the last time, these values are really way below what we're actually seeing, actually going to propose as a reference level.

CHAIRPERSON FROINES: I'm sorry for interrupting. I'm the one who said not to. I just had one quick --

DR. BROWN: You're allowed.

CHAIRPERSON FROINES: One quick question is do you have data like this from southern California?

DR. BROWN: I don't think -- well, it probably is available. But it wasn't presented in a nice slide like this. So I'd have to dig it out. We could probably get it. We had presented data on southern California in the past previous meetings for other chemicals. I thought this would make a nice change to do something on the Bay Area.

PANEL MEMBER BLANC: I think it's relevant because I think Southern California has done a very good job in air monitoring at the time of compilations of refinery sites, whereas Northern California Bay Area is quite deficient in that.

So I would actually add to John's comment that there was some very fragmentary core sampling done at the

time of the recent Richmond fire, Chevron fire. And you should -- and since that was within the time frame of datas we were doing through August, I think you need to get those data.

And I think Alan has some comments on this table in your document and ways in which it's problem laden as well. So we'll come back to that.

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DR. BROWN: This is a scheme of the metabolism of butadiene as seen in rodents and what's known in humans -- it's sort of a composite slide.

The main reactions going on are oxidation of butadiene to an epoxide hydrolysis to dyall (phonetic) and then conjugation with glutathione to various intermediates.

Three epoxides are formed. And generally all of the epoxides and possibly also the hydroxy methyl phenyl keytone are thought to be capable of reacting with DNA and protein. Two of the metabolites are well enough known to urine to be characterized M1 and M2.

The form of connect models we've used in the document and that are detailed in the appendix include about five of these metabolites. It's a fairly interesting metabolism, the three different epoxides

shown.

The main ones we're interested in are the mono epoxide, the one, two epoxy, three butane, and the diepoxybutane.

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DR. BROWN: Acute toxicity in animals. The key study we used here was Hackett, et al, 1987. In the original report, which we released to the public, the study is based on 78 pregnant female mice exposed to zero, 40, 200, or 1,000 parts per million butadiene for six hours a days on gestation days 6 through 15.

Significant dose dependent reduction of fetal body weight was observed in males at a P value of less than .05. The authors originally identified a LOAEL of 40 parts per million. And we, in our analysis, did a benchmark dose and got a value of 13.4 parts per million, which was equivalent to a human equivalent concentration of 22.5 parts per million. We used an overall uncertainty factor on this value of 100 to propose initially a value of 225 parts per billion, or .5 per meter cubed.

In our initial public comments, we got a very extensive reanalysis of this data provided by ACC. I think the work was done in Dupont, a 150-page statistical analysis, which more or less refuted the LOAEL of 40 parts per million and established a new LOAEL of 200.

Using this data, which I'll show you in a few slides, we re-did the benchmark dose and got a slightly higher value, about 30 percent high, or 17.7 parts per million and an HEC of 29.7.

So using the same overall uncertainty, we calculated about 30 percent higher value of 279 parts per million, or .66 mgs per meter cubed, which we're proposing as the acute REL.

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DR. BROWN: And this summarizes that derivation based on the reanalysis of the Hackett data with a BMCL of five. This is a 95 percent lower bound on the 5 percent response level. 17.7 parts per million HEC of 29.7. These are dosimetric adjustment factors for animals to human conversion here of 1.68.

There are various uncertainty factors we use here. We discussed before, they are basically described in more detail in our guidance, which we put in the document about ten years ago. In this case, the cumulative uncertainty factor comes to 100. And our final value is 29.7 divided by 100, or 297 parts per billion.

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DR. BROWN: Now the analysis -- I hope you can read this. This is the original analysis, which shows the supposed LOAEL at 40. And the key values here are the

males in the pup body weight going from 1.38 down to 1.06. And the reanalysis was done in a lot more detail. Involved an analysis of covariants, which is described -- I think it's on page 14 of the document. I only devoted about a paragraph to describe what was done, which really doesn't do justice to a 150-page report that they submitted. But essentially, I was convinced that this new analysis was probably better to use, even though we didn't base it on a NOAEL/LOAEL approach. We're using a benchmark dose, which uses all of the dose response data and a statistical analysis of the lower bound on the five percent response level, but you can see in this reanalysis, the values are not vastly different, but they do make a difference in the dose response analysis by benchmark dose. We ended up with a 30 percent higher value based on these reanalyzed of data in this more extensive statistical analysis.

PANEL MEMBER BLANC: Question, Chair.

This analysis is going to come back to be a major point of discussion, I anticipate. So consistent with your request, I'm not going to say anything now. But my lack of asking something now doesn't mean that I accept what's being said.

CHAIRPERSON FROINES: I don't think there is any question that the Green/Hackett studies are going to be a

major point of discussion. So forewarned as -- whatever that expression is.

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DR. BROWN: Okay. We're forewarned.

This gives a little more detail. The new data is shown in red. The original data, this was all done at the top of the slide here with the applied dose. We tried a number of models. The Hill model gave the best fit initially, with the 13.4. The reanalysis using the Green data also with the Hill model, 17.7.

We tried some other metrics here. We did some modeling on this, but none of the models seem to give an improvement on the applied dose, so we stayed with the applied dose for this treatment on the acute.

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DR. BROWN: Now the eight-hour REL, here we have different studies. We use the NTP 1993 supported by Doerr, et al, 1996. This is a -- the NTP study is a huge study with hundreds of animals. Many doses -- I think it was five doses, plus the control. Many time intervals where animals were sacrificed throughout the study. It was really a Tour de Force in terms of toxicological analysis.

The exposure was inhalation at zero, 6.25, 20, 62.5, 200, and 625. Essentially, locks it at six hours a

day for five days a week for various periods up to 103 weeks. This was -- you can look at this as the sort of non-cancer side of a cancer study where they were doing both things at the same time.

The toxic affect we focused on here was the dose dependent increase in ovarian atrophy. We calculated a benchmark dose of BMCL05 of 1.01 parts per million based on those.

The time adjustment was not continuous. It was less than continuous for an eight-hour. And we used the same sort of human equivalent concentration adjustment using a DAF of 1.68. And we have more or less the same overall uncertainty calculation of 100, giving a final value of 12.7 parts per billion, or 28 micrograms per meter cubed.

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DR. BROWN: Now a little more detail. I hope you can see this slide.

We actually took different -- analyzed different time points throughout the study. This is for ovarian atrophy in female mice during a two-year study. We had data at nine months, 15 months, and 24 months.

And I think we could get some fit to the nine-month data, but the 15 and 24 month we couldn't get fits without taking data out of the top data. So we tried

something different. We wanted to include all of the data in an analysis. So we tried to do a -- sort of a time weighted regression. And there's a couple of asterisks on the left-hand in the bottom there. I couldn't include the footnote on this slide because it was too big. But it's on the bottom of page 24, if you wanted to look at that.

Essentially, we took the data, which was additionally in quanta form, and we converted it to continuous equivalents. Did our fitting with a non-linear regression using the times in months as the weight. And then we took the fitted values, convert it back to quantal, and then to benchmark dose on that. And we got two fits: A log probic and a log logistic. Both gave statistically significant fits.

There's not much to choose between these two of fits statistically. But we choose the lower value, the 1.01 as being slightly more health protective. That's the value that we based our derivation on in the previous slide. That's the 1.01 you see on this slide.

Now, this is detailed of four tables in the appendix that give the gory details of this analysis if you wanted to look at that. But essentially, this is not a very fancy thing. It's sort of a weight averaging approach of these three different curves, but averaging using all of the data, the 435 animals in the analysis.

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DR. BROWN: Now, the Dohr supporting study is completely different. Here is a study where you have female mice that are injected intraperitoneally with doses of butadiene, mono oxide at five different doses every day for 30 days, ten animals per dose. Same thing for the butadiene diepoxide: Ten animals per dose, five doses every day for 30 days.

The endpoint, at the end of the study, animals were sacrificed. You're looking at decrease in ovarian weight and decrease in uterine weight.

For decrease in ovarian weight with BMO and DEB respectively, the weight drops are .04 to .02. And with DEB, .0375 to .015.

For uterine weights with BMO, .27 to .1. And for DEB, .34 to .03.

Now, we used internal dosimetry using a pharmacokinetic model here, and the metrics we chose were the area under the curve of the monoepoxide in blood and the area under the curve of the diepoxide in blood.

The model also looked at hemoglobin adducts, and all these were done with simulated intraperitoneal doses.

The best fit we could find was for the ovarian atrophy endpoint was the area under the curve of the diepoxide that was dosed with the monoepoxides. So you're

injecting monoepoxide and you're actually measuring the diepoxide.

CHAIRPERSON FROINES: Say that again. I missed it.

DR. BROWN: The best fit we could find for the endpoint, which in this case was ovarian atrophy rather than uterine atrophy was the area under the curve of the diepoxide obtained from injecting the monoepoxide.

So if you can view it as you're putting in one metabolite and you're getting the next metabolite out. That was the one that gave the best fit to the ovarian atrophy. With the polynomial model, we got a fit of .92, which is a very, very high degree of accuracy of the foot.

And the BMCL05 in this case is an area under the curve. It was 20.5 microohmes per liter times hours per day. That was the dose metric that was equivalent to the five percent response level, 95 percent lower bound on that.

That's not very useful. So we actually had to use the model to find out what the external equivalent of butadiene for a six-hour exposure was for that. So we sort of back calculated from the 20.5 to find out what concentration of butadiene would be equivalent of that, and we got 1.8 parts per million.

I was surprised by this, because this is a vastly

different approach than the 15, 24-month exposure to the animals. This is a 30-day exposure. But this value is very close to the 1.01 and even closer to the 1.58 parts per million we had from the NTP study. We think this is pretty good supporting evidence of the initial value that we chose for the eight-hour REL.

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DR. BROWN: Now, the only difference between the chronic REL and the eight-hour REL, we use the same studies, the same essential approach, was we used a continuous averaging to get the final value. In other words, we use six over 24 hours times five over seven days, assuming a worst case. That this was a continuous exposure situation. And we get a lower value, hence, we use the same overall uncertainty factors. But now the final value is three parts per billion and 6.7 micrograms per cubic meter. That's basically the approach we took to get the chronic REL.

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DR. BROWN: Overall summary, all of these effects are developmental. The acute REL, .66 milligrams per liter cubed. The eight-hour REL, 28 micrograms per meter cubed. And the chronic REL, seven micrograms per meter cubed.

That ends the sort of the technical presentation.

I do have additional slides on the comments we received from the ACC, if you'd like me to go through those.

CHAIRPERSON FROINES: Please.

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DR. BROWN: The first comment obviously was the Hackett, et al.

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CHAIRPERSON FROINES: One question. Just so -- we have the unfortunate situation in so far as we got three documents from the ACC two days ago.

DR. BROWN: Yes, I received them.

CHAIRPERSON FROINES: And we had not seen previous documents, so that we don't have the benefit of the previous documents, and we have a document for which we had basically one day to read it. So when you're talking about comments received, you have to give us the context so we understand.

DR. BROWN: Okay. These comments were received in July, I believe. These are not all the comments. These are the comments I picked out as being ones I thought were sort of significant or, you know, that I responded to.

I'm surprised to hear you say you didn't receive that. I don't know what happened there.

CHAIRPERSON FROINES: Am I wrong? I got mine on

Monday.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: The comments which Joe is going through here were provided along with the report, which you received from us a few weeks ago. So --

PANEL MEMBER HAMMOND: We didn't actually get the comments. We got the comments as extracted. We got the extracted comments.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: You got the extracted comments.

CHAIRPERSON FROINES: It seems like we're a step behind in the process.

PANEL MEMBER HAMMOND: Usually, we get the actual comments; right?

CHAIRPERSON FROINES: Yeah. Absolutely.

DR. BROWN: I can't understand it myself.

The comments that were received yesterday, I saw 3:00 yesterday afternoon. So they're as new to me as they are you. But they appear at least --

PANEL MEMBER HAMMOND: The comments you're talking about now are the comments that were here from July. And usually we receive the actual comments.

DR. BROWN: Yeah.

CHAIRPERSON FROINES: Yes.

DR. BROWN: I don't understand what's going on.

CHAIRPERSON FROINES: Absolutely.

DR. BROWN: Anyway, okay. So these are extracted comments that I put together myself for this presentation. They're not all of the comments. But they're the ones that I thought were important.

The first one was the Hackett. The comment essentially was that Hackett used inadequate statistics to identify a LOAEL for the male fetal weight. And the Green analysis 40 PPM as a NOAEL, not a LOAEL.

Our response to that was we essentially agree the re-analysis shows that value is a NOAEL. However, our derivation is not based on a NOAEL approach, but rather a benchmark dose method that uses the entire dose response to derive an alternative to the NOAEL, namely, a BMCL of five.

In our graph, this value was 13.4. With the Green re-analyzed data, the BMCL of five is 17.7, about a 30 percent higher value. This would increase the proposed aREL to 297 from 225. That was our response to that.

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DR. BROWN: The next comment -- the draft states that most of the environmental releases of butadiene are associated with fugitive or accidental emission during manufacture, use, transport, storage, or disposal. The U.S. Environmental Protection Agency reports 1.6 percent

of the environmental emissions of butadiene are from industrial production and use; 78.8 percent from mobile sources, and 19.9 percent from other miscellaneous combustion sources and they cite EPA 2002.

Our response was the text refers to point sources as the primary focus of the Hot Spots Program. We said the sentence would be revised to clearly distinguish contributions from point and nonpoint or mobile sources of butadiene emissions. And we've done that in the revised document.

CHAIRPERSON FROINES: I asked the question about Southern California for a reason. And the reason is the amount of butadiene in the air in Southern California I believe is substantial.

And so this notion of 78.8 percent from mobile sources, we're talking about significant emissions from mobile sources. So that needs to be understood that this is not -- this is not Houston, Texas with chemical factories. This is an issue of transportation.

DR. BROWN: Sure. Sure. But our Hot Spots Program is still our Hot Spots Program.

CHAIRPERSON FROINES: I understand. It doesn't mean that you can't acknowledge the significant emissions that may be occurring.

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DR. BROWN: Comment 3: The draft states, "Misclassification of VOC exposures may have occurred for some chemicals, such as formaldehyde, with important indoor sources. But data from other studies support the view that motor vehicle emissions strongly influence the exposures to other VOCs, such as benzene, ethyl benzene, toluene, xylene, and probably butadiene."

And they bolded this for emphasis. There's nothing in the text that warrants the inclusion of butadiene in the sentence. And thus, the reference to butadiene should be removed.

Our response was -- and they're referring to a specific paper that I was citing in the document.

OEHHA believes the sentence in question is a reasonable extension to related volatile compounds included in the study. In their discussion -- I'm referring to the author's discussion on page 652, the authors clearly state, "Although confidence intervals were wider, odds ratios were positive for symptoms scores greater than one in relation to concentrations of the same VOCs, as well as 1,3-butadine.

Even the author mentioned that, so I didn't think we had to change that.

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DR. BROWN: Comment 4: OEHHA selected ovarian

atrophy in mice as the key non-cancer health effect for butadiene to derive the eight-hour and chronic REL. While the Owen, et al, 1987 publication indicated that only gonads were examined, the original study report shows ovarian atrophy was observed in two of 46 control rats and 1 of 24 rats in 8,000 per million exposure group. They cite the table 24 page in this report.

Thus, it appears that ovarian atrophy is an effect specific to the mouse and likely a consequence of the mouse's high rate of butadiene metabolism compared to other species. Given available knowledge of interspecies difference in metabolism, the selected endpoint is of questionable human relevance.

Our response was that the ovarian atrophy in the female mice in the NTP study was the most sensitive non-neoplastic effect noted among several organ weight effects, lung, liver, and kidney, and uterine, testicular, and nasal olfactory epithelial atrophies.

It is difficult to extrapolate toxic effects between rodent species, much less between rodents and humans. OEHHA does not accept the notion that studies in mice are not relevant to human risk assessment, nor that rats are necessarily more human than mice. So that was our response to that.

CHAIRPERSON FROINES: That's always a good one.

Depending upon what your perspective is. People think humans are mice and humans are rats.

DR. BROWN: Comment five: The REL for chronic exposure to butadiene includes an interspecies uncertainty factor of 30, which included an uncertainty factor of ten for toxicokinetics. However, OEHHA provides a minimal justification for the selection of this value. The document should be updated to include greater justification for the selection of uncertainty factor based on the available database.

Our response was the use of the UF of 10 for intraspecies uncertainty in toxicokinetics is based on OEHHA's guidance developed in response to the California Children's Environmental Health Act of 1999. And this is in OEHHA 2001. We have a document on this in our guidance.

Unless we have adequate information on all segments of the exposed population, we must acknowledge the uncertainty and apply a larger UFTK. As noted in the draft, the human metabolism butadiene is based on studies in relatively few deceased adults. For example, Duescher and Elfarra 1994. And in our view is insufficient to encompass the possible range of metabolism and toxicokinetics, particularly in young children.

So that was our response to that. And as I said,

that goes back to our guidance on this subject.

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DR. BROWN: Comment 6: Significant evidence is provided that this diepoxide metabolite is produced in the mouse in far greater quantities than any other species, including and especially humans, with limited conclusive evidence that humans can produce this metabolite at all.

This information should inform OEHHA regarding the magnitude of specific interspecies uncertainty factor related to the interspecies differences pertaining to ovarian atrophy and argues strongly that this value should be less than one.

Our response is we have reduced our usual uncertainty sub-factor for toxicokinetics from 10 to one based on the published evidence of greater metabolism of butadiene to epoxide metabolites in the mouse compared to results with other species. Human data on this point are relatively limited. At this time, OEHHA does not favor the use of fractional UFs, or uncertainty factors.

As noted above, the ovarian atrophy endpoint was the most sensitive observed in the experimental animals. Our assessment does not assume that this is the exact effect that will occur in exposed humans. Butadiene exposure caused many other toxic effects that may be more relevant to humans. This is part of the uncertainty.

So that's the last slide I had on the comments.

There were some other comments. I don't know why you didn't get them.

CHAIRPERSON FROINES: Well, the only other thing I would raise and others might want to raise is there was the publication by Kierman and Grand that we received --

DR. BROWN: That's the one that I received at 3:00 yesterday afternoon.

CHAIRPERSON FROINES: So the problem is this is a fairly substantial document. And I don't know what to do with a document which has so much analysis and we don't have the benefit of being able to review it.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I think with the publication -- I also have seen this study at 3:00 yesterday afternoon. I think it's unfortunate that we weren't given more notice of these comments. I'm not quite sure what the purpose of sending them so late is, unless it's merely to confuse the situation. Because it certainly doesn't contribute to our ability to make a rational analysis of the material.

But I think I'm right in saying that paper is basically a published account of a risk assessment which was done for the Texas Department of Environmental Quality. And although this publication is something which has arrived -- so we are, in fact, familiar with that

Texas report. And --

DR. BROWN: Actually, it's cited in the document.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: It's cited in the document.

DR. BROWN: We discussed it.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: We have discussed that, the Texas analysis.

DR. BROWN: I think the new analysis goes farther though. I've just been able to eyeball some of the figures in it. And I think they have a range of values going up to 20 parts per million as a chronic RFC, which is orders of magnitude 10,000 times higher than what we're proposing.

So some of the methodology doesn't make sense to me. I think they're using a BMCL 01, which may not be supported by some animal data. So I need to see the data they're using. We can use an 01 on epidemiological data sometime where you have thousands of large N, but I don't know if the power of their statistical studies would support a BMCL 01. But I don't know. I have to see the details of what they did.

It's a very large paper. As I said, I just skimmed it and looked for the bottom line to see how it compared to what we're doing or what they did in the past, which we cited in our document.

Their previous number was only three times higher than ours. And it was based on one uncertainty factor in the analysis. Their use of one over root 10 instead of one for the interspecies. As they said, they used a fractional uncertainty factor. That gave them a value that was about three times higher than ours. Now how they're going to use this new data in Texas, I don't know. This is just a publication at this point.

PANEL MEMBER RITZ: Can I say something?

I don't see any new data in this. This is a meta analysis based on already published data. So what you see here is a reanalysis of the existing data. If you had looked at the existing data, your point of view is your analysis is probably any other --

DR. BROWN: Our analysis is certainly different. We use a pharmacokinetic approach. In some respects, it's a completely different analysis.

Now, in some cases, in the past, Texas has used the same study that we used here, the NTP study and the DPA used, but different methodology. And those numbers were somewhat different, but they weren't orders of magnitude different. They were like a factor of two or three different. They were not 10,000 times different.

CHAIRPERSON FROINES: I don't know how to -- I think Beate's point is well taken.

But the point being that it would be useful if we knew what papers have you been -- have you evaluated because I don't know if there are documents missing that might have shed some light on these issues. So Beate's point I think is right on that it would be useful to -- or my interpretation anyway -- it would be useful to have a better sense of what was evaluated from your standpoint.

DR. BROWN: We could certainly include our review of this paper in our revision. We're going to have comments here that revise the document and we can bring it up to date.

But looking at it, I don't know if we change any numbers. It's too early to tell.

But we did review their earlier effort. I think it's Grant, et al, in the references, and gave a short discussion of it toward the end of the document comparing it also with EPA's values.

So I think that's a value they already have in play in Texas. So they have to change something. I just don't know. I'm not familiar with Texas regulatory affairs. At this stage, it's just another paper that I reviewed in terms of methodology.

CHAIRPERSON FROINES: So Dave, are you finished with your presentation? So we should go to the Panel?

AIR BRANCH CHIEF SIEGLE: Yes. We're finished.

CHAIRPERSON FROINES: The lead person for this document is Alan Buckpitt. And so I think we should start out with his comments.

PANEL MEMBER BUCKPITT: Okay. Good morning.

Please remember that I'm a chemist toxicologist, not a statistician. So I will be dependent on my statistical colleagues for anything more than the key test.

I thought the document overall was well written and laid out the case for the RELS selected and really focused on the most sensitive endpoints.

I'd like the Committee to understand that if you look at the literature for butadiene, it is extensive. You're talking about thousands of papers. So there is a lot there, clearly.

The document that we're reviewing doesn't have a thousand references in it. I think many of the important ones were included with the document.

The one thing that I would encourage us to at least consider is some of the very recent work that's been published on bio markers. So I think if we could all agree that butadiene is clearly metabolized as several different metabolites that looks like the butadiene. Diepoxide is deriving the acute endpoints to the agent.

Much owing to the work of Jim Sputnig and his

colleagues, we now have a couple of very good markers for that that have been looked at in mice, rats, and humans. So we should be able to get an estimate of how those species looked together. It's not going to change the numbers that have been used in the document. But I think it makes a firmer basis for us to make some judgment on.

If you look at the formation of that diepoxide, it's really based on a complex set of factors. You have the generation of the monoepoxide. That can again go to the dyall (phonetic). It can go further to the diepoxide. Those can both be conjugated with butadiene. Your species' differences become very complex in terms of looking at the throughput of the parent compound to that diepoxide.

You can measure diepoxide in the blood. Some studies were done I guess just a couple years ago looking at the AUCs for this, the illumination of half lives and distribution of half lives. So it's pretty short half life. You have something that has a half life or distribution of a half life of about three minutes, illumination and half life of 14 minutes.

So looking at the parent epoxide in the blood, I don't think it gives us an integrated measure of the total form. I think we're better off with our endpoint measurements, either with hemoglobin or the bis DNA that

are generated.

So what I'd like to suggest that the Committee take a look at is the use of some of these newer studies, either looking at the amounts of diepoxide bound to the internal availing of hemoglobin or to the amounts bound to the DNA. I know our purpose isn't to look at the butadienicity and partial carcinogenicity of this compound. It's really more the toxicity. But I think these can inform us in terms of the amounts of metabolite integrated and formed over time. I think it might be a better measure for us.

I think a very significant paper published just a couple months ago in analytical chemistry looked at both the formation of the bis 71 and the valine adducts and hemoglobin.

And the thing I'd like to point out, if you look at the amount of addict generated per PPM of butadiene, what you see is that at the very low concentrations, essentially the efficiency of throughput doesn't change. And that's important.

Normally, if you're dealing with the dose response, as you lower the dose, you lower the amount generated. And you get to a point where you fall under the KM so your response curve drops off.

This doesn't do that. It looks like the

catalytic throughput at your low dose is again divided by dose remains the same for those low doses. And as you go up in dose, it becomes much less. So extrapolating from high to low is going to result I think in aberrant numbers.

If you look at -- and there are data published again about six, nine months ago, at very low levels, there is detectable levels -- comment six from ACC I think is incorrect. There are detectable levels of the butadiene diepoxide bound at hemoglobin adducts.

The other comments that I had were really pretty minor. IAR has done an update for butadiene. They list it as a Group 1. So it used to be 2B. And then they upgraded that to 2A in 2008. When I checked, they had a supplemental publication to Group 1.

CHAIRPERSON FROINES: It's one. And that's very important. Although this is not a carcinogenic document, but that error stood out like a sore thumb. So we can change it easy.

PANEL MEMBER BUCKPITT: Again, I think all of these are easily changed.

If you look at your table that you presented on the error levels in Northern California, the one thing that we really need, what is the minimum detectable level. And I didn't -- did I see that?

DR. BROWN: I have a column there percent less than, but I don't have the actual table.

PANEL MEMBER BUCKPITT: I think it would be important in all of that discussion to include that.

There was some discussion of cite 452(B)(1).

CHAIRPERSON FROINES: Can I stop you for a second? I'm sorry.

The data from Northern California, I would be interested in knowing -- and you might put it as a footnote someplace -- what was the analytical methodology that was used to collect those values? Because there are significant losses of material, especially, for example, with transportation sources. So we need to make sure that the analytical capability is adequate.

DR. BROWN: I'll go back and do more.

PANEL MEMBER BUCKPITT: I think that would be worthwhile.

DR. BROWN: Both for this and for the southern California.

PANEL MEMBER BUCKPITT: So the report focuses on P452(B)(1) as the primary enzyme that catalyzes the activation of butadiene and the monodiepoxides. That's likely correct. But I would -- and I don't have the data to back it up. But butadiene looks like styrene, looks like naturalene, looks like dichloroethylene. It's where

you get this mouse to rat to human difference. And the differences are -- I mean, they're ten fold. The rat, ten fold. And across all three of those chemicals, if you look at the data in the literature, it's consistent.

I think there may be other enzymes associated with that activation. And there's no data at all, but I think 2F might be involved. And I say 2F because it metabolizes styrene. It metabolizes dichloroethylene. It's a very catalytically efficient enzyme that exists in very high levels in mouse lung and nasal tissue and pretty low levels in the rat. So it could account for those differences.

The material on David Lewis's modeling, normally when they list the SIPS, they will give it a new sub-family name if it catalytically is different. So the valine to -- I can't remember what the residues were. Valine to lysine differences, I'm not sure are going to make catalytic differences. I don't think that's ever been shown. So as far as I know, those differences don't make any catalytic difference. If you know better, then speak up.

The only other comment -- and it's minor -- top of page 13, you talked about particle bound. And I thought the way this was phrased was confusing. Seems like the chemicals dissolved in the fluids and then

diffuse. And I think that's where --

CHAIRPERSON FROINES: I'm sorry. This is important to me.

PANEL MEMBER BUCKPITT: Right. So it was at the top of page 13. And it's maybe my own lack of -- "combustion of butadiene were different taken up and investigators found that the combustion generated ultra fine particles migrated from culture medium through the" -- let me repeat this.

"Investigators found that the combustion-generated ultra fine particles migrated from culture medium through the cell membrane but not into the cell interior. The organic chemicals bound to the particles, however, were found to migrate from the particle surface through the cell membrane into the cytosol."

And I'd simply say that it defused off of or dissolved off of the particle and moved in.

CHAIRPERSON FROINES: No.

PANEL MEMBER BUCKPITT: If it didn't.

CHAIRPERSON FROINES: But I would argue we have electro micrographs that I could show you that shows ultra fine particles penetrating epithelial cells ending up in the mitochondria and the nucleus and the cytosol.

So there is no question whatsoever that these

particles, which contain the butadiene -- which may contain the butadiene on the surface and then the butadiene can be hydrolyzed off and do its damage. So the ultra fine issue with butadiene is really quite an important one, with a lot of chemicals. I mean, it's not just butadiene.

DR. BROWN: So do you support this change in the text?

CHAIRPERSON FROINES: Which one?

PANEL MEMBER BUCKPITT: I think what you need to do is go back and maybe cite more modern data on particles and the dissolution of chemicals from those particles.

But the question that I have for you, John, is does the butadiene diffuse from the particle before it enters the cell? I agree. Particles get into the cells.

The question is: Is the butadiene diffusing across as butadiene or is it released once the particle is in the cell? And do you know?

CHAIRPERSON FROINES: You know we have a lot of lung lining fluid and there is a potential for dissolving things off.

So the answer to your question is I would guess that there is a proportion that is in -- stays on the cell surface and a portion that is actually taken up by the cell.

PANEL MEMBER BUCKPITT: And the reason this would be important is that it really controls the disposition of some of this material. That's what I have.

CHAIRPERSON FROINES: Bill.

PANEL MEMBER NAZAROFF: Just to come back to this one point because it's an important one.

I don't know the answer to this, but my expectation is given the low molecular weight, high vapor pressure of the species that we actually would not find much butadiene that is particle associated in normal circumstances is going to be predominantly in the gas phase.

So to head down this path, I'd like to see some evidence presented that butadiene partitioning onto particles is, in fact, a real concern, that it's been detected or it's believed to be there from a physical chemical argument.

CHAIRPERSON FROINES: I think you are 100 percent correct. I think that the likelihood -- I mean, I think that we get exposed to butadiene in the vapor phase. We don't necessarily get it -- we get exposed by particle absorption or particle -- well, observed -- you know what I'm saying.

PANEL MEMBER HAMMOND: The sentence there is talking about the products of the incomplete combustion of

butadiene itself. So apparently there are some particle phase products of the combustion of butadiene. I don't know.

PANEL MEMBER NAZAROFF: You're right.

PANEL MEMBER BUCKPITT: I haven't looked at the paper. I can't remember it.

CHAIRPERSON FROINES: So I would say there's probably going to be some balance obviously between the vapor phase and the particle phase. And if you have a 10, 20 nanometer particle, you may have -- may be adequate to have some butadiene and stick to it, so to speak.

PANEL MEMBER NAZAROFF: John, I've not studied butadiene in this context, but I've studied other organic chemicals in this context. And for a species whose molecular weight is only 50 or 60 grams per ohm, it would just be extraordinary circumstances. Like exorbitantly high particle presence before you would expect significant partitioning of some species with that low a molecular weight into the particle phase.

CHAIRPERSON FROINES: Don't misunderstand. I'm arguing, I think, that it's going to be in the vapor phase. But to the degree that there is anything in ultra fines, that's an issue.

But I agree with you. I think that you're going to find it in a vapor phase with that molecular weight.

Your turn.

PANEL MEMBER BUCKPITT: That's it.

CHAIRPERSON FROINES: Okay.

PANEL MEMBER BLANC: So I have a question for Alan.

I'm not quite sure how any nuance of the metabolism would impact their benchmark calculations. So what I need to hear from them is in terms of the assumptions of their model for the benchmark calculation, whether or not it presumes a linearity of dose response and then what it does when you get below a certain level. Does it take into account a potential model fit that would suggest a greater efficiency at a lower level of delivered dose.

DR. BROWN: Are we talking about the particle versus vapor?

PANEL MEMBER BLANC: No. I don't care anything about the particle argument at all. I'm talking about your acute derivation of your acute REL and how does any of the metabolic issues play into that.

I could understand how also it could possibly play into some of your animal to man extrapolations. But that's not the critical thing I think in your benchmark calculation.

DR. BROWN: Well, as I said before, we looked at

some pharmacokinetic analysis, but we didn't find any advantage to it over the applied dose in terms of --

PANEL MEMBER BLANC: Did that pharmacokinetic modeling that you tested presume their relationship that Alan was mentioning?

PANEL MEMBER BUCKPITT: I think the issue here is that related to those low doses and the efficiency of --

DR. BROWN: Well, these weren't low doses. This was a study done at 4200 to a thousand parts per million butadiene. Those are not low doses.

PANEL MEMBER BUCKPITT: Right. Exactly.

So what we're seeing, if you look at your rats and mice and subsequently humans, that little bit of data that we have is that those low doses, the efficiency, if you will, is essentially stable. And then as you go to higher doses, the amount of the adduct generated per PPM of butadiene.

So I think Paul is making a very good point. As you extrapolate from those high doses, which is what you used --

DR. BROWN: We're extrapolating linearly.

PANEL MEMBER BUCKPITT: Exactly. Is there a way of dealing with this business of as you get down to low dose the --

CHIEF SALMON: Technically speaking, we're not using the model which is fit by the benchmark method as the extrapolation tool. We are using the uncertainty factors as the extrapolation tool.

So in that sense, we are making a default assumption, which, in fact, is entirely consistent with your comments on the linearity at low doses. That's what we assumed.

PANEL MEMBER BLANC: That's the interspecies factor; right? It didn't --

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Inter and intra.

PANEL MEMBER BLANC: So the answer is, therefore, those issues are addressed in that, but the bottle itself assumes -- the benchmark calculation assumes a linearity.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: The benchmark calculation is designed only to fit the data in the range of observation.

PANEL MEMBER BLANC: Now, let me return to that point.

I think you might wish to make a further statement then that invokes the data he's citing as further support for your interspecies, since -- and intraspecies, since that seemed to be an issue that was raised by the industry representatives.

Now let me return to the data at hand for the acute REL calculation.

I'm trying to get my hands around what the implications of the re-calculated data are in practice. The re-calculation was not taking the raw data and modifying it. Wasn't the re-calculation just how they compared the dose levels across each other? What else did they do to the data?

DR. BROWN: Well, as I understand it -- I'm not a statistician. So I tried to wade through this large document and focus on the key parts of it.

They claim that by doing this analysis of covariants using I think it was litter size and sex ratio as the key covariants, they were able to find a different level of significance for that.

PANEL MEMBER BLANC: Yeah. I understand that. But why would that change the raw data?

DR. BROWN: It doesn't change the raw data.

PANEL MEMBER BLANC: So why is there any difference in your model between using the raw data and using the raw data. What is it you're using in your benchmark that would in some way be different? Because I understand you came out with a 30 percent different result, and I can't understand why the result would change at all.

DR. BROWN: This is the original data. And that's --

PANEL MEMBER BLANC: That's just rounding. That's just the absence of rounding. What is it that's different?

DR. BROWN: Well --

PANEL MEMBER BLANC: They're this same data. Are you telling me using non-rounded data changed by 30 percent your estimated benchmark?

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: The data which go into the benchmark modeler are -- actually, the group means and variants, those are the inputs to the model, which is fit.

In this case, they did an analysis of the individual animal data which accounted for the between litter effects and so on. That enhanced calculation, if you like, by separating out the individual variability and the litter effects would actually produce a slightly different value for the variants, which is then going to be input into the benchmark model.

But as you see, the effect is not very large. It essentially it's an effect on the amounts of variation that's accounted for, rather than anything effecting the -- if you like, the best fit estimate. But we are -- in this case for our benchmark, we are using the lower

confidence limit on the benchmark. So the --

PANEL MEMBER BLANC: So you're saying what changed is your confidence intervals narrowed.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: They're changed by using this more complex analysis, which includes within and between group variants analysis. That's the only difference.

PANEL MEMBER BLANC: So why would you do that if you're only using the male data? I can understand why you would do that if you use the values for the combined population. Do you believe that the female and male dose response has a different slope in this study? Have you tested whether there is a significant difference between the male and the female offspring butadiene dose response?

DR. BROWN: Well, I think the male gave a better dose response. You can see from the average values they're both significant.

PANEL MEMBER BLANC: You're not answering my question.

DR. BROWN: What was the question again?

PANEL MEMBER BLANC: Do you believe the slope is statistically different between the males and the females in this dose response?

DR. BROWN: I can't say. I know we used the males.

PANEL MEMBER BLANC: They only used the male. If you only use the males, don't use the covariants adjusted with the females. It's not logical to me.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I don't think that's what we're -- I think the covariants adjustment is for the between litter effects. But it's divided up by sex as well.

So how did they do that? I mean, the intent of the Green analysis was to account for within group variation as opposed to taking each effect group -- and I think we're talking about the effect group as the males and females were considered separately from the word go. But I think that the intent of the Green analysis was to separate out the within litter versus overall variants, which produces a slightly different result.

PANEL MEMBER BLANC: Well, I suggest -- I would like to request that you have some statistical consultation on what you've done. And I would like you to at least look at and comment, even if you don't do it, on how using all of the data would change what your calculation is.

If you want to make the argument it's ultimately more conservative public health protectively to use just the male data, that's fine. But I think you need to comment on why it is that if the two slopes are the same

that, in fact, it's not -- you wouldn't get more confidence in your benchmark calculation by using all the data together.

DR. BROWN: It's not just the slope. It's the lower bottom. You can get pretty big differences from relatively small changes. I've seen this in other studies.

I think we have done the females, not with the Green analysis, but with the original. I think we choose the males over the females. I think it gave a better fit.

I can go back and look that again. I haven't done the females with this re-analysis. I can certainly try that. I can try both.

PANEL MEMBER BLANC: Yeah. I wouldn't suggest doing -- there is no gain to doing the female separately. But I do think you should look at what happens to your model and your model fit when you use all of it together. Pool the data if you believe there is fundamentally a very parallel response.

PANEL MEMBER HAMMOND: In the document, on page 14, you state that the data sets for combined sexes in female fetal weights gave similar results.

DR. BROWN: I think they did.

PANEL MEMBER HAMMOND: That would seem to me you did do those.

And, in fact, I thought that the combination came about only because of doing the Green analysis, that you had done male and female separately before that so that would seem to me also that you should increase your statistical power by combining them.

DR. BROWN: You'll go back and look at it again.

PANEL MEMBER BLANC: So that was for me --

CHAIRPERSON FROINES: Is it clear what Paul wants from you folks?

DR. BROWN: I think so.

PANEL MEMBER BLANC: Now, what I'm saying may or may not make you change your actual recommended REL. It might just appear as text that explains --

DR. BROWN: I don't think it's going to change the number very much, but it would --

PANEL MEMBER BLANC: It could change the number and it could stick with the number you have. It could not change the number and you use that as being more reasonable and you say, by the way, if you did just the males, we got the same number.

It could change the number and use that number and say here's why, but we have done this. Because the text that you're referring to doesn't refer to the benchmark calculation, which only comes later when they do it.

CHAIRPERSON FROINES: Benchmark comes much later.

PANEL MEMBER BLANC: So that's on that.

I said I would return to the Northern California data and its presentation. It's obvious from the table that your minimum detection limit is .025 parts per million. That's clear.

Actually, as I understand it, their current minimum detection limit is more sensitive at .009 parts per billion. And therefore, using 2008 data doesn't make much sense. So if you're going to present data even if it's northern or southern California, not only should you make clear what the detection limit is as was set already, but you should use more recent data that will have less samples. Won't have places where 100 percent of the samples are non-detectable.

So that's on that. I think it's a minor point. But anyway, it is of the genre of the error about the IARC status. It does undermine -- you come across something like that and you say, well, okay. This I stumbled upon. What else is off?

So that brings me to the flip side of Alan's comment about the very large data set that's out there, the very large number of publications and how do you systematically review the literature in that situation or how do you convince -- how do you present convincingly

it's not an idiosyncratic review of the literature, which you don't want to give that impression.

One of the problems I had with this document is that there is an awful lot here that's still a review of carcinogenesis and butagenesis, which is -- and there is no argument as to why any of that is actually relevant to the health effects, the non-cancer endpoints that you want to focus on.

So if there was some way of talking about electrophilic metabolites and their non-toxic endpoints a bit more explicitly than you do and about oxidated stress and its health impacts other than carcinogenesis, I think that would be fine. And if you wanted to say and we are not going to be reviewing any of the literature related to this substance and cancer and butagenesis except in so far as it may relate to other non-cancer endpoints, that would make it clearer.

Now, that being said, my own brief review, which I like to do before these meetings, am I coming across stuff that's not being talked about? So, you know, there is an entire review out there on the cardiovascular toxicity of butadiene from a theoretical point of view. I wasn't somewhere where I could access the paper. It's very likely that it's highly theoretical, that review. None the less, someone has bothered to write an entire

review in recent years about cardiovascular outcomes and you're writing a non-cancer adverse outcomes document, you at least need to say there has been a review of this subject and it hypothesized the following, but there aren't any data to support it. I mean, come on, guys.

And similarly, there is a paper. It's not a very good paper, but it's a paper that looked at people, humans, after a major industrial release of butadiene and compared them to reference and looked at neuro psych outcomes. It's not a great paper. But you can't not cite it. You can cite it and say, "This paper, we didn't use the data because there was no, you know, measured level and we didn't like the reference," or whatever. But to not refer to it at all is counterproductive and undermines your article.

And also the whole issue of butadiene releases, of which there have been apparently many over time historically -- Texas being the big player. But there have been big conflagrations of large public releases of butadiene. I think that's very relevant to say somewhere that that has happened. This is not theoretical.

Again, coming back to this experience with Richmond fire, the one thing that they measured appropriately was acrolein which was above your REL. And they said there was no elevation above the REL. They just

misstated the reality. So these RELS could certainly come into play in that kind of situation.

I do think that the introductory section was really hard to wade through in terms of where it was that you were thinking that 1,3-butadiene was coming from. I don't know whether a table would help that. I know you got caught up in this thing about what proportion comes from here or there. But I didn't get a sense are we talking about butadiene, when it comes out of a car, is it because it's in gasoline to start with? Is it because it's created when you have a combustion of gasoline? Is it both? I wasn't clear, in fires, that you allude to, again, just natural fires, so is it like acrolein? Is it something that is created as a combustion byproduct? If so, how much?

These are all things that matter to this kind of document very much to me from a public health point of view. I couldn't get a sense of any of that. I was wading through a jar of marshmallow. The more I read, the less I understood.

I also, by the way, think one sentence about butadiene in -- not just in butadiene styrene copolymers, but butadiene as a feedstock, if it is a feedstock, in synthetic rubber for chlorination, what's the relationship between chloroprene and butadiene? What's the

relationship -- which is chlorinated butadiene, isn't it, essentially? And also isoprene, which is ethylated --

CHAIRPERSON FROINES: Chloroprene only has three carbons.

PANEL MEMBER BLANC: And this has four?

CHAIRPERSON FROINES: Uh-huh.

PANEL MEMBER BLANC: So then I'm not clear. So make it slightly -- that could be two sentences. That's a minor thing. But it either presumes too much or too little on the part of the reader.

CHAIRPERSON FROINES: May I make one --

PANEL MEMBER BLANC: Let me just -- I think I'm very near finishing up.

CHAIRPERSON FROINES: Please, go ahead.

PANEL MEMBER BLANC: So this issue about how you reviewed the literature and what you included and what you didn't include and was it just your -- how you were feeling that day or was there some methodology to it really needs to be stated.

I don't -- just like Alan, I do not expect a thousand references. But actually since, you know, 950 of those were about carcinogenesis and are irrelevant essentially, I don't actually think it's going to be that hard for you. I think almost any reference which is about a non-cancer endpoint needs to be addressed in some way,

unless it's from the Yugoslavian literature from 1956 and the Russian ones about the immunology of whatever.

CHAIRPERSON FROINES: Can I make one comment, Kathy, before I call on you?

I think Paul's point is very interesting. You know this debate focuses on butadiene's carcinogenicity and the debate around the metabolism has been going on since 1980, as far as I can tell. Ron Melnick and others debated it in the '80s. And so we've been given a plethora of discussion on butadiene and its metabolism. Since we don't know any mechanisms, all we can do is assume that some of that might be relevant. And probably undoubtedly is.

But the point is that we don't have the road map for what happens in the cell with butadiene as it leads to downstream health effects. And so finding documents like the cardiovascular review helps look at the signaling pathways, the transcription factors, inflammation, and so on, so forth. I mean, there is a lot of -- if there is some mechanistic data that would be very useful, especially as it relates to health endpoints. And we don't have that in this document.

And there is such an emphasis on immunogenicity dominent lethal effects and metabolism that it's not clear to me we're just not missing the forest through the trees

in some respects. And I know it's hard because there are so many papers and they're so related to carcinogenesis it makes it very difficult. So these comments are appropriate, but I think they're really quite important actually.

And Kathy, I'm sorry.

PANEL MEMBER HAMMOND: That's okay.

CHAIRPERSON FROINES: I finished my thing and I went to sleep.

PANEL MEMBER HAMMOND: That's all right.

So my comments relate to the exposure section. And I have a few concerns there.

First of all, if this is supposed to be reflective of what are the exposures of Californians and how that -- whatever your RELS how they relate, I do think this is along the lines of what Paul said there needs to be a better information. Particularly since you are coming up with acute RELS, we need to be talking about what are some of the acute exposures. And so neo refineries, that may be some of the issues and some of the refinery incidents.

And I guess I don't understand enough and recognizing I'm in a funny place here and probably should know this, but I know you brought this up as a hot spot. It's under the hot spot legislation.

Do we do -- we're supposed to be judging on toxic air contaminants. We're not trying to say this is a toxic air contaminant or not at this point, but is that correct? What are we trying --

CHAIRPERSON FROINES: It is a toxic air contaminant from the standpoint of carcinogenesis.

PANEL MEMBER HAMMOND: Are we being asked as a panel to decide whether it's a toxic air contaminant for non-cancer or just --

CHAIRPERSON FROINES: No.

PANEL MEMBER HAMMOND: Just to accept RELS that they're suggesting.

CHAIRPERSON FROINES: That's right.

PANEL MEMBER HAMMOND: For the RELS that are suggested, it is important to be looking at these one hour and eight hour exposures that can happen. And is it true that under the hot spot legislation, that a freeway then is not a hot spot? Is that the understanding? That's not the understanding. So would a freeway of -- I mean, I just don't really know that legislation.

CHAIRPERSON FROINES: A freeway can be a hot spot.

PANEL MEMBER HAMMOND: So I think we need to be aware of that.

The presentation on exposures, like Table 1 --

first of all, I definitely agree we need to have other parts of the state included. But these are mostly I suspect are long-term averages rather than one-hour and eight-hour averages. We need to talk about some of the particular events that can happen.

Go ahead.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I was just going to say, technically speaking, the hot spot regulations relate specifically to stationary sources. Not things going down the freeway.

But having said that, the air modeling techniques which are used for stationary sources have also been deployed to deal with linear sources. And there are various things which are sort of intermediate factors, like distribution centers and rail yards and things like that, which do count as at least point sources.

So the methodology which we're developing here is specifically related to the Hot Spots Program and the stationary sources. But it actually gets deployed on a more extended basis for related issues.

PANEL MEMBER HAMMOND: Including, as you said here, secondhand smoke.

CHAIRPERSON FROINES: And just to draw this to a conclusion --

PANEL MEMBER HAMMOND: I have a couple more

things.

CHAIRPERSON FROINES: I'm not taking away from you. I just want to make a policy conclusion.

As far as I'm concerned, we can address transportation, mobile sources, goods movement, those kinds of issues, within the context of the hot spots legislation. And I'm assuming that that is a policy decision. And I assume that Gina would agree that we should. I don't --

PANEL MEMBER NAZAROFF: Did you say can or cannot?

CHAIRPERSON FROINES: That we can.

PANEL MEMBER NAZAROFF: We can, yes.

CHAIRPERSON FROINES: We're able to address transportation within the context of hot spots. I don't want to put you on the spot, Gene. We'll just talk about it here.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I think the reality is you have to remember the actual use and implementation of all these things is not either in our hands or that of the Air Resources Board. It's in the hands of the local air districts. And they have a number of individual district programs where they use the hot spots information to inform the kind of programs which they're implementing locally. So to a

considerable extent, it's a question of giving the air districts the ammunition which they want for their purpose.

CHAIRPERSON FROINES: So for purposes of this discussion, we will assume that transportation is relevant and we can get going, move on now. Kathy.

PANEL MEMBER HAMMOND: Okay. One very small point, but it makes it easier to read for people, if you pick one kind of metric to give for the air concentration. So such as parts per billion as opposed the micrograms per cubic meter.

I mean, now, if you feel you want to quote what's in a paper, then you could put the other one in parentheses. But most readers would be able to follow it easier. I know how to do the conversion. But I just think -- it's a pain in the neck for me to go down and write them in as I'm trying to look at numbers and things. So it's just a suggestion to make a more readable document.

And then I wanted to ask why you were discussing occupational exposures. Are occupational exposures relevant to the exposure portion of the document?

DR. BROWN: I think we probably view the eight-hour value as something that might be applicable in exposure or school type situations where you're getting

periodic exposure.

PANEL MEMBER HAMMOND: That's fine. I personally would like to be seeing more occupational exposures included in these. And it's an understanding again of where Californians are exposed.

So to the degree again in the exposure section of the document, you talk about toll workers and Baltimore tunnels -- Baltimore harbors. And you have some numbers there. Those numbers actually look pretty small. But later in the document when you're talking about some other studies that were done, there are occupational exposures referred to within the studies that are orders of magnitude higher than these. So if you're going to have some discussion what exposures people experience, I think it's very important to include those high exposures within this section.

CHAIRPERSON FROINES: I would just say, given our experience that Paul and you and I had with methyl iodide, I would actually put in a paragraph that talks about the fact that people don't work eight hours. They work longer hours. And so if you have to keep in mind that, yes, the eight hours is traditional, but we should recognize that it's not cast in stone either.

PANEL MEMBER HAMMOND: Is the eight-hour REL -- is the purpose of an eight-hour REL to be related to

occupational exposures? I know that is the ozone eight-hour --

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Within the Hot Spots Program, it's designed to address the needs of protection of off-site workers. In other words, people who are in an occupational context, but not actually within the plant boundary, but over the fence and at work. That it's specific context in the program. It may have other uses besides, of course.

PANEL MEMBER HAMMOND: So I guess I would also say I understand that CalOSHA is outside of this agency. But it's always useful when an agency is doing a lot of scientific work, which this clearly represents, that the document be as useful as possible for other agencies that may trigger some of that.

PANEL MEMBER BLANC: I forgot to bring this up or ask about it.

Your usage of the separate terms point source, area source, and mobile source, what was area source? Is that an accepted category?

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: As well, I think the term point source, area source, and linear source relate specifically to the type of air dispersion modeling which is being done. The critical distinction within terms of the program needs is

the stationary sources versus the mobile sources. So those are two different dimensions.

PANEL MEMBER BLANC: So if you drew a diagram, they would not be a -- event diagram of mobile sources and stationary sources, that would be the universe.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Right.

PANEL MEMBER BLANC: Is that correct?

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Yes.

PANEL MEMBER BLANC: So a forest fire would be a stationary source.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Forest fire, I'm not quite sure where a forest fire fits in this.

PANEL MEMBER BLANC: A refinery fire.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: A refinery fire would be a stationary situation.

PANEL MEMBER BLANC: And it would be a stationary area source?

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Depends how big it was.

PANEL MEMBER BLANC: That's where I'm getting at. If you did a word search in your document and started

looking up where you're using area source, point source, mobile source, it certainly isn't in the context of who is going to do the modeling, whether it's going to be linear or stationary.

So if you could either clean it up and be more consistent or somehow -- because I was surprised to see -- I didn't know when you used it, are you trying to tell me something? Because -- and I think it's particularly relevant for this chemical because of some of the sources are likely to be in conflagration of various sorts.

And similarly, I think it might be worth saying explicitly that this material is typically used under pressure as a pressurized gas or liquid -- a liquid because it's under such pressure. Because haven't a lot of the releases historically been the rupture of pressurized 1,3-butadiene type lines or containment things, to use the technical term?

DR. BROWN: Well, we mentioned fugitive leaks. I know I attended a seminar on butadiene when I first started studying this 25 years ago. There was a lot of talk about fugitive -- getting valves that not leak butadiene. I think that was --

PANEL MEMBER BLANC: But it comes down to the physical properties of this thing, which it's a gas. And if you work with it industrially, it's typically

pressurized.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: It's handled under pressure in a supposedly sealed but occasionally not plant.

PANEL MEMBER BLANC: So I think I'm not talking about a page about this. But when you're talking about the physical properties of the thing, it's also -- doesn't it also self polymerize and explode? Don't you think that's something you should say?

Again, all these things come to the sort of the exposure scenarios that would tend to happen with this material that would then expose the general public.

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: Yeah, I just wanted --

CHAIRPERSON FROINES: We're bringing up the heavy weights now.

OEHHA SCIENTIFIC AFFAIRS DEPUTY DIRECTOR MARTY: I don't know how much I weigh.

I just want to bring the Panel back a little bit, just looking historically. What we're trying to do with the RELS exposure levels is dose response assessment. So OEHHA does not get involved at all in exposure assessment. That's done by the Air Board and by the local air pollution control districts.

We used to just have a very little bit on

exposure, just kind of very surface. This is what butadiene is used for, and this is how it gets into the air typically. And over the last few years, we've been asked to expand that more and more. To me, it's becoming more of a distraction than not. So what we really need is for people -- the Panel to focus on the dose response assessment piece and did we do that right. So I just wanted to throw that out there.

PANEL MEMBER BLANC: Well, again, I think what we've been saying has to do with a very modest amount of text and probably removing some of the text that's there. And I wouldn't mind if you did it in a table frankly. It doesn't have to be four pages.

CHAIRPERSON FROINES: Beate.

PANEL MEMBER RITZ: Thank you, Melanie, because I think my points are to the dose response question.

I see again and again the reference to significance and significance testing. And we all know that we can make anything significant if we have a large enough sample size, even the smallest effect.

When I look at these tables 2.2 B, I see dose response written all over. And even though the 40 PPM and 40 level was not statistically significant and the upper confidence interval included the null, it's meaningless if you're trying to estimate a dose response. And I would

highly recommend not to use these kind of criteria to evaluate data. We are really after a dose response. And the lower level, if you add a few mice, you will probably get a different confidence level.

PANEL MEMBER BLANC: Not to interrupt you. That's why they did the benchmark. I think what they did was implied that they were somehow being influenced by this re-analysis, which was completely irrelevant to their ultimate correct decision to use benchmark dosing, which is specifically a way of doing what you said.

PANEL MEMBER RITZ: That's what I understand. But the document doesn't read that way.

PANEL MEMBER BLANC: It gives the wrong impression.

PANEL MEMBER RITZ: Right. And so also when you're referring --

CHAIRPERSON FROINES: Is that clear to you, what she said? Because Paul and she were going back and forth. I just want to make sure OEHHA understands what her point was.

DR. BROWN: Could we get it again, please? I'm not sure how clear it is.

PANEL MEMBER RITZ: So the document reads as if you're looking at each value on its own, rather than trying to extrapolate a dose response and using a whole

data, what you have in the whole data as relevant.

I think you used it correctly, but the document reads as if you have made significance testing evaluations of lower limits, et cetera, that are based on just one strata, the 40 PPM. When, in reality, you probably used a whole study.

DR. BROWN: The whole thing, all of the doses are used.

PANEL MEMBER RITZ: That's what we were going back and forth on.

The other is when you cite confidence intervals, you really need to give both the upper and lower limit. Otherwise, just call it an upper confidence limit. So otherwise, it's not just a phrasing issue.

So apart from that, I'm also wondering when you talk a lot about metabolism and whether that's different between species and I don't see anything about differences between humans and who are the humans that actually contributed to the evaluation of the metabolism for this one gene. We know there are for some proteins, there are 40 and 100 fold differences between humans. Makes me a little worried, because do we have the ideal human here that we are measuring?

We also know that their life phase differences in how proteins activated or how they work. For children,

for pregnant women; there may be huge differences in elderly. None of that has been mentioned. But there is a lot of rats and mice in here. I just wanted to say maybe going back to the humans and the differences in humans, at least in a sentence I would like to see.

CHAIRPERSON FROINES: So from my standpoint, what I want to make sure is that Beate just mentioned a number of topics. And we need you to understand what she's asking you to do in the document, not she's making intellectual points. But the question is how does that effect the document itself.

PANEL MEMBER BLANC: Well, doesn't the ten-fold intraspecies factor take that into account?

I think the question is, on rare instances, we have recommended that in addition to the ten-fold interspecies and ten-fold intraspecies factor that we use to take into account what you're saying, there have been rare instances where we have urged an additional safety factor because of extraordinary evidence of either greater than ten-fold differences within species or particular lack of evidence.

I don't feel that there's data here that pushes me to urge them to go beyond the 100-fold ten times ten difference. So I want to make sure that you're not feeling there is, because they do take that into account.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: We are using a value of ten for the toxicokinetic component of the interspecies uncertainty factor, which follows our guidelines, but is three times greater than what was being recommended in the previous guidelines precisely because of the sorts of uncertainties that you have referred to. I think we're certainly recognizant of that. We have, in fact, got this provision built into our basic guidelines to address that.

I think possibly what we need to do is say that's justified because this didn't receive a lot of comments simply because it's already been discussed at considerable length in the guidelines. This is a known problem.

But we should probably in citing that as the choice for that UFHK, we should cite the known data suggesting that is a very extensive variation among humans.

And also the frequently raised argument by people saying that mice make 10 or 100 times more of something than people do is typically based on a selection of half a dozen catalyst, which is clearly not representative of the living population.

PANEL MEMBER RITZ: That's fine. I just would like to see it in here, as we said.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT

CHIEF SALMON: I think we know where we need to say that at this point.

PANEL MEMBER RITZ: And just one last question. When I read so much about ovarian atrophy, I'm really getting worried about the F2 generation effect, but I gather there is absolutely no literature on that; right?

DR. BROWN: I didn't see it.

CHAIRPERSON FROINES: Are you done? Bill.

PANEL MEMBER NAZAROFF: So I don't have a lot to contribute this time around, but a few comments.

Not withstanding Melanie's plea, I'm going to come back to exposure. And part of the reason is that, I mean, there are a couple ways we can think about this. One is you could exclude all considerations of exposure from documents of this sort. But I think that would be doing a disservice to the function of the document. And these people read these not just because they're interested in the statistics that support a particular REL or not. They also read these to get some background about an environmental contaminant of concern. And I found them helpful, by the way, historically in this regard. So I'd like to retain that function. So if we are going to do it, we should do it well. If you're going to do it and we're going to review it, it should be done well.

So during the -- this hadn't occurred to me

before. But during the meeting this morning while others were offering their comment, I did some Google and web of science work and came to a couple of points that I'd like to suggest for your attention.

The first is there are a good sample of butadiene data from the South Coast air basin. They were collected under the MATES Program. The latest version of the MATES Program was --

CHAIRPERSON FROINES: MATES IV was about to start, as I understand.

PANEL MEMBER NAZAROFF: This is MATES III. And the butadiene numbers from the earlier version of MATES, which was sampling in the 1990s, were about an order of magnitude higher than your reporting for Northern California, .4 parts per billion is sort of central tendency result.

MATES III from 2005 through 2007, something like that, showed about two-thirds reduction in atmospheric levels of butadiene roughly consistent with improvements that we've seen in other motor vehicle associated primary pollutant emissions.

So you know it's easy -- that's an easy set of data to add some information about. I'd love to see something from the Central Valley where air pollution problems are quite severe. And I don't have a good sense

of whether butadiene would be better or worse. But I don't know of a particular source of data from the valley.

I think Kathy's comment about trying to identify -- and I don't know any such data acute -- information about acute releases and what the consequent concentrations were would be helpful to have something.

Second comment to offer -- and this -- I mean, this first one I think could be addressed relatively easily. The second one, quite easily, has to do with a few words about the atmospheric life cycle of butadiene that it's, A, only emitted from primary sources. It's not formed as an atmospheric byproduct or a byproduct of photochemistry in the atmosphere.

B -- I think that's true, but it ought to be confirmed.

B. That its lifetime in the atmosphere is not long. It's in the range of an hour to ten hours, depending on photo oxidation conditions.

And C. What is the primary means by which it's degraded. I'm not absolutely sure, but I think it's OH radical attack.

Just some points there to help anchor the conversations that we know when we're concerned about it in southern California, we don't have to worry about it blowing out to the desert and just doesn't live that long

in the atmosphere.

And then my third point is there are areas where some polish is warranted just to improve clarity and thoroughness of documentation. And I'll pass along my detailed notes after I have a chance to transcribe them because they're not legible to anybody but me right now. But just as illustrations in the second paragraph under occurrence and exposure, there are several very specific statements made without references. And there needed to be some citations to the specific points made.

And then when I got to the end of the document reading the development or the derivation of the reference exposure levels, some of the acronyms I know. Some of them I could kind of guess at. And AOC I only learned about this morning, area under the curve. Just needs to be a little more attention to the poor reader, who is not --

DR. BROWN: There is a jargon to this business.

PANEL MEMBER NAZAROFF: The jargon got a little deep in places. And this is the part that I think needs to be most clearly understood by people.

So again, I'll provide some specific suggestions along those lines. Those are all of my comments.

CHAIRPERSON FROINES: Thank you. Those are very relevant.

And just to keep asking the same question, what he said you got in terms of what you need to do at this stage?

DR. BROWN: Yes.

CHAIRPERSON FROINES: I mean, if somebody finishes talking and it's Greek, tell us so we can rephrase it.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: We look forward to receiving your detailed comments.

CHAIRPERSON FROINES: Okay. Jesús.

PANEL MEMBER ARAUJO: I have a number of points.

I'd like to start with Paul's comment on the lack of mentioning of some of the non-carcinogenic effects of the butadiene. And so you mentioned that you found the reporting important and there was a theoretical consideration for cardiovascular disease and even a reviewer mentioned that that was possibility.

So it's actually a lot more than that. There are several publications and dates back to 1996 there was a publication not in an obscure journal. It's in circulation where it was reported that butadiene could -- at the moment was the first component from the cigarette smoke that was shown to have broad impacts and effects.

And I notice that in your report -- let me just

go in the actual report. In the section corresponding to the chronic affects to the humans, which is on page 23, at the end of your first paragraph in the second half, you mentioned basically it was observed workers during the period 1964 to 1972 and the increase in mortality, emphysema and cardiovascular diseases, chronic rheumatic, and arthrosclerosis disease among the subjects.

There was no -- any mentioning or why such an important statement was completely ignored. And in the sense that, well, there was a report of increasing cardiovascular diseases. How there was no follow up on that and how you concluded there was no cardiovascular and arthrosclerosis effects.

So I will certainly suggest to include some of those citations.

One other thing would the study from the Arthur Payne 1996, he put out a review of mutation research in 2007, and there is another study in 2004 where they showed the very significant effects of the butadiene, oxidated stress and mitochondria effects, et cetera, which suggests that effects may go beyond the main changes in the ovarian atrophy that you considered.

CHAIRPERSON FROINES: Can I ask you one thing? Just one thing.

The point about oxidative stress that you just

raised and associated with it is that there is clearly a mechanistic pathway -- metabolic pathway leading to potential for oxidative stress. That's really not addressed.

PANEL MEMBER ARAUJO: Yeah. Absolutely.

CHAIRPERSON FROINES: Go ahead.

PANEL MEMBER ARAUJO: So the second point I'd like to make is that in the way how the report is written, it appears as if the only way how this product, this compound can produce toxicity is by the generation of some metabolites and use by the SIP once and the iso science. However, when I was looking at the review from Arthur Payne about the cardiovascular effects --

PANEL MEMBER BLANC: That's the paper I was referring to. I never got to see the paper, just the abstract.

PANEL MEMBER ARAUJO: In that paper, they mention -- they cite another paper where the effects of the butadiene are not in relation to the levels -- metabolized from the butadiene, monoxide or the dioxide. They actually took livers from those animals and measured those compounds, and there were no increase in those compounds in the same animals that were having an increase. They proposed that these toxicity may be exerted by other compounds differently to these compounds,

that we're attributing to most of the raises. I think this is a very important point because I have to say that one of the comments --

CHAIRPERSON FROINES: You're saying other compounds, not butadiene.

PANEL MEMBER HAMMOND: Other metabolites?

PANEL MEMBER ARAUJO: Other metabolites different to those that are traditionally responsible or considered responsible for the toxicity.

I can even bring the specific. They say the plaque from activity of the butadiene is not associated with the butadiene monoepoxide or the diepoxide tables and may be associated with the generation of an as yet unidentified metabolite.

The reason why I think that this is important is when I read the comment from the ACC, American Chemistry Council, and I read the letters, and I going into the study that they sent us, I have to say I was almost convinced that all the arguments that they put about the differences between the mice and the humans. And the data really in the companion paper is quite compelling that we shouldn't be using mouse and rat data to make our conclusions, just because they completely lack connection to the rats and the humans. And they make a lot of assumptions in here.

But some of the assumptions has to do with toxicity, how the toxicity caused, and the formations of the adducts, et cetera. We consider that the toxicity is not necessarily chose by those compounds. We cannot make a conclusion that based on the lack of or elevation in these metabolites, we cannot conceive any potential toxicity.

The other point has to do with Beate's comment about the importance of mentioning on the human data. And that comes also in the same review where they mention about the importance -- or the potential importance of human polymers in all the genes and enzymes associated or responsible for the metabolism of the butadiene. So they refer to the polymer for the GFC1, GFC2, the SIP2, 1, (phonetic) all in relation to the cardiovascular disease which may in a way set the stage to consider maybe the butadiene could cause more significant cardiovascular effects on people who have these polymers.

So since I have a special interest in the cardiovascular diseases and also given the importance of the cigarette smoke and the secondhand smoke and environmental tobacco smoking and the butadiene can be one of the important toxic components of the cigarette smoke, I wonder how do we really differentiate the butadiene in the environment that is due to the environmental tobacco

versus the butadiene from other sources you were mentioning and whether when we're talking about the RELS should we take into consideration places where the environmental tobacco smoke is a heavy, has high concentrations, like if you go to bars, for instance, what are the concentrations of the butadiene in those places. I don't know whether it's ever been measured and whether we could be in compliant according to the levels that we are citing now, because it is a major component of the RELS.

So I think that may be better explanation or consideration of these links with the cigarette and how you separate one versus the other.

CHAIRPERSON FROINES: Can I be the policeman? And that is that, again, we need you to tell them what you would like them to come back to us with so that it's not ambiguous. So I think what you've just said is very clear, but I just want to make sure that they are saying, "I understand what Jesús is asking us for."

DR. BROWN: Yes, I get the idea. You know, we'd love to find a human data set we could use on butadiene, and we'll certainly look at the cardiovascular literature and see if there is anything there and discuss that as well.

CHAIRPERSON FROINES: I mean, Ralph Delphino's

work, which you do quote, but sort of do this with your hand, that work may not be usable, but it's not irrelevant.

DR. BROWN: Right. It's can be discussed, even if we can't use it for dose response.

CHAIRPERSON FROINES: I understand that. But it relates to the fact that there should be a comment about their asthma, cardiovascular disease, other endpoints that need further investigation. And I think that's what Jesús is saying, too.

PANEL MEMBER BLANC: I do think the issue, the challenge of the epidemiologic data for this substance is that frequently it is in the context of multiple exposures, and that that limits the Delphino work as well, because those were exposures that was ambient air pollution exposure. So butadiene was but one substance. And clearly with cigarette smoke, it's an issue. And it's an issue even at the industrial exposure literature where often there's co-exposure to styrene if it's styrene butadiene flammable. That's been more of a bugaboo for the cancer literature.

But I think that a couple of sentences that actually say that in one place about the limitations and challenges of data sets that involve multiple exposures is critical.

CHAIRPERSON FROINES: Paul, but all I'm trying to say is we've had three people, and to some extent Kathy, raise issues about epidemiologic endpoints. And we just need to make sure it's adequately covered in the document.

PANEL MEMBER BLANC: Oh, yeah. I agree with that.

And also I think Jesus's point that there could be a parallel between cardiovascular endpoint adverse outcomes and the health outcome that you are using for your eight hour and chronic REL. I think that should be also said explicitly if you agree with that as a mechanistic implication.

I was going to suggest because, Alan, you were the sole lead on this document. And I think that for the next revision, it would be helpful if Jesús -- if the Chair would agree -- if you would be co-lead in reviewing it. So you would have more of a major role in looking at this revision.

CHAIRPERSON FROINES: The Chair agrees. Hopefully, the participate, Dr. Jesús will agree. And if so, we'll go ahead with that.

PANEL MEMBER BLANC: Join Alan in that role.

PANEL MEMBER ARAUJO: Is that --

PANEL MEMBER BUCKPITT: That's fine. You betcha.

PANEL MEMBER ARAUJO: Sure.

CHAIRPERSON FROINES: We always -- Beate, your time is coming.

PANEL MEMBER RITZ: Yeah. Yeah.

CHAIRPERSON FROINES: We always have two leads on a chemical.

And where are we? So basically I think you're feeling confident that you know what needs to be done for the next draft?

DR. BROWN: I think so. It always helps when we get the official transcript to go through and see if we missed anything.

CHAIRPERSON FROINES: Oh, that's a good point.

PANEL MEMBER ARAUJO: Just to reemphasize on Paul's comment, I believe that that study, which I actually have here but I haven't had a chance to read in any detail, the study from 1996 should be analyzed in details because it can be the basis for. And then you have to decide whether it could be the basis for regulation or not and whether the study you have for the atrophy or the ovary atrophy will be a better study.

DR. BROWN: Do you have the details of this study?

PANEL MEMBER ARAUJO: Yeah. I can give the citation.

CHAIRPERSON FROINES: Araujo and I can write a

mechanism that gives you reactive oxygen, oxidated stress. And I will write it, but you obviously can't put it in your document, but it might be interesting for you to take a look at.

So I think we're done with this chemical.

PANEL MEMBER BLANC: Could I just ask one other question? And maybe Melanie would know this.

In terms of how frequently you've ended up being forced to use the same study to generate both your eight hour and chronic your REL, does that happen with some frequency? Is this quite an outliar or is this --

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: We haven't, of course, done a huge number of eight hour RELS at this point. But it's quite common that we use the same studies for the eight hour and for the chronic. The idea being they are related in that the eight hour is expected to be protective of repeating exposures, not necessarily lifetime, but on a repeating basis. And it often happens that we do -- it's not invariable, but it --

PANEL MEMBER BLANC: There's precedence for it.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: There's precedence for it, definitely.

PANEL MEMBER ARAUJO: One last comment. And it's just a writing style. In relation to the recent or what

you term "recent" studies or "recently." And in most of the cases, it is appropriate. But you're saying more recent studies or recently. But in a couple of places, you need to be careful because you're citing two recent studies and the studies are from 1998 or a recent study from 2006. Those are eight years ago.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: When you're as old as Joe and I are, recent becomes a flexible concept.

DR. BROWN: Another point is these documents go through sort of a gestation period. And in this case, we had multiple authorships on it as well, so which adds some problems. So I think we are working on it. We'll go through that.

CHAIRPERSON FROINES: Well, I think this has been a very good discussion. From the Chair's standpoint, seeing the fact that everybody had relevant comments is good. It's more work for you. But hopefully it will work out for a better document in the end.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I'm sorry. I have a brief comment to follow once you're done with the document.

CHAIRPERSON FROINES: Please.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: If we are through with butadiene, I wanted

to, if we had the time, just very briefly mention to the panel some of the things that we've got coming down the road over the next six months or so. Is this a good moment to address that or would you rather I waited?

PANEL MEMBER BLANC: I would like -- if we just get a sense. We have one other thing that's on the agenda, which is discussing whether or not this panel would consider oral testimony.

I think you have to leave soon. So if that's going to be a brief discussion, it would be great if you would be here for it.

PANEL MEMBER HAMMOND: I did have one other thing I wanted to mention. That is I understood that we had to get written comments at least two weeks before our meetings. I felt that was something we had true in the past.

CHAIRPERSON FROINES: You're absolutely right. That was a policy that we established some years ago. And then I was told by legal counsel that industry can submit or anybody can submit anything right up to the meeting. So I would have been basically told -- and Jim can correct me if I'm wrong -- but I've been told they can send it the day before. So that's the bottom line.

I think, for example, with ACCC, Jim ought to take a minute and talk to them and say we would like this

not to happen again because it's inappropriate. But you can't cover every public body or corporation to get that kind of agreement.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: The ACC comments were received by e-mail sometime yesterday by us. And it would appear from the timing of the e-mail that was, in fact, sent probably within an hour or two of close of business on the east coast yesterday.

CHAIRPERSON FROINES: Well, you know, the Panel has the right -- the Panel could have said in this meeting today we got these things a day ahead. We didn't have time to read them, so we're not going to talk about them.

But the trouble is we have a group of people who are hard working, so they did look at them. But we have the option to say go fly a kite.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Our approach is simply we try to deal with it as best we can.

But it's quite obvious that the intent of the that mode and timing of submission is to minimize our opportunity to make constructive comment on the issue. And to a large extent, they succeeded.

PANEL MEMBER BLANC: But I think that's a good segue to the next item, if we could discuss that before

Andy tells us about what's coming down the pipeline.

CHAIRPERSON FROINES: But I just want to say that we will -- if we get comments late, we'll do the best we can. And if we can't do them, we won't. So we will deal with it as we best can within the limited time frame we have.

So go ahead, Andy.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Do you want to segue?

PANEL MEMBER BLANC: My discussion is he not do his presentation of what's coming down the pipe and we discuss the oral testimony issue.

CHAIRPERSON FROINES: Oh, I'm sorry. I missed that, didn't I?

Okay. So this is a matter for the panel, not for OEHHA.

There has been a request by a citizen that we, this Panel, take verbal testimony. The Panel has been in existence since 1983. So what's that? Thirty-three years or 30 something.

PANEL MEMBER NAZAROFF: Almost 30, 29.

CHAIRPERSON FROINES: And during that time, we have never taken public commentary. We felt that it was more effective for the level of work that goes on with this Panel that taking public testimony as well would

defeat the quality of the work and the efficiency of the Panel. So we have never taken public testimony.

There is a law -- and I'll read it to you. The law on toxic air contaminants, which created this Panel, is found in Chapter 3.5, Article 3, of the Health and Safety Code, and contains such a conflicting -- contains the following provision. "This law provides that any person may submit any information for consideration by the SRP which may, at its discretion -- at its discretion, receive oral testimony."

Now, there is another law, the Bagley-Keene Open Meeting Act, which says that meetings should allow for the public to testify. So there is -- on a legal basis, there is a contradiction.

However, it would appear that it's up to us to decide whether we want oral testimony. And so we need to decide -- we need to decide whether or not we want oral testimony. And Paul has been on the Committee the longest besides me and so I'll ask him to comment based on his experience.

PANEL MEMBER BLANC: I think the person writing the request is of the opinion that having such testimony would assist our deliberations, and I do not believe that would be the case.

I would be strongly opposed to a set and standard

policy of oral testimony for brief periods. We certainly have had invited scientific experts to come at various times and present information for the purposes of aiding our discussion. And that was at our discretion and may arise again. But that's a very different context and content than an open mike presentation.

We have gone through a period of diminishing resources where the meetings in and of themselves are less frequent and where the resources provided for the State for having the meetings conveniently and not just in Sacramento be taken away. And I think this would just further compromise our function and to take up very valuable time that we don't have.

We serve essentially as volunteers with per diem. It takes us away from our other. Work coming to Sacramento makes it more odious. And so I would oppose this in as strong as possible terms. I would oppose any change in the status quo in the strongest possible terms.

CHAIRPERSON FROINES: Kathy, you've been the second longest person. I can't speak to Stan. I could hint, but I won't.

PANEL MEMBER HAMMOND: In general, I tend to feel that it's good to receive input from as many people as possible. That's my basic bias in doing this. From that point of view, I would be in favor of it.

However, I share Paul's concern quite deeply that this is a Committee that has a lot of work to do with very limited time. All of us are extremely busy. And I'm going to have to leave shortly for another prior commitment. So it's really hard for us to get to do the work that we have to do, and I just don't see how we would have time to be taking oral testimony.

If there were a need for it, perhaps provision could be made that some people could make oral testimony before some State employees who could videotape it and that could be available to those that want to look at it. But I think for our time together, we need to use that for the interactions that I find relevant.

CHAIRPERSON FROINES: Just for the information of people who are newer, when we did diesel exhaust in 1998, we actually held a public workshop, and we had guest speakers from a wide range of disciplines. And it was very effective. And we had the option that we had thought we wanted a workshop on butadiene. There's nothing to --

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: They were two workshops on butadiene REL, which we held during public comment period.

CHAIRPERSON FROINES: All I'm saying --

PANEL MEMBER HAMMOND: There always are. Actually, that's a very good point Andy brought up. They

always have -- there are always public meetings where people can speak about these. And this is information in a way that doesn't come to the Panel.

CHAIRPERSON FROINES: That is a very good point, but I want to emphasize that we, as a Panel, had a workshop. It was our workshop. We invited the speakers. And we -- so, yes, there were diesel. God, I don't know how many workshops there were that you guys put on. So there's always been workshops or discussions. But in this case, I'm just simply referring to the Panel itself.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Would the Panel be interested in a greater level of participation in the regular workshops which we organize already?

PANEL MEMBER BLANC: No.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Okay.

CHAIRPERSON FROINES: I think it's up to the individual.

PANEL MEMBER HAMMOND: Just be informed of them.

CHAIRPERSON FROINES: I don't want to -- I'll give Beate, the new person the chance.

Bill.

PANEL MEMBER NAZAROFF: So I don't have a lot to add, except to make my views I guess known.

I think Paul expressed ideas that I share, although with greater vigor than I would have expressed them myself. And I share Kathy's perspective that government should be open in so far as we can make it open. But I think in the instance of the operation of this Committee, we accept all things written. I think that's as open as we need to be. And so I would favor maintaining the way we've been operating.

CHAIRPERSON FROINES: Thank you.

Jesús.

PANEL MEMBER ARAUJO: Yeah. I also agree with comments that have been expressed.

And one concern though is whether what they're trying to do is that they can find, like, a better way of communicating their points to the Panel, which sometimes in the written mode it is difficult to just write it. And I don't know whether they could perceive the Panel is not being responsive to what they're asking.

So I wonder whether it is something that could be between the lines with these requests. And if they're asking -- for instance, suggest to the Panel address this or does that. And so maybe we should in those instances be more explicit because of the specific point they're making and respond even directly to the people who are addressing us. So in that way so they can be some

improvement in the communication without opening the channel for the less desirable comments to the Panel.

CHAIRPERSON FROINES: So I'm hearing you say we won't have oral testimony, but we'll find ways where we can improve the communication with the external bodies. I'm not sure that would work. Help me here.

PANEL MEMBER ARAUJO: Yeah, what you're saying is exactly right. I agree in not taking the available testimony, but exploring on ways how the Panel can communicate better with the petitioners, so with the people who have questions. And whether it is that we make an effort in addressing the questions as someone asks and we make a response. And that is going to be certainly recorded.

Or -- I mean, what I'm seeing is many times the comments are already addressed by OEHHA. And we find them that they -- an address has been made to the comments is satisfactory so there is no need to discuss them. And perhaps the people who are raising those questions would want the Panel to discuss the points in the record.

PANEL MEMBER BLANC: We do. It's reflected in our record.

And I think the way I would interpret your point is that we should always be sensitive to when we get the presentation from OEHHA, their responses to the comments

which are almost universally corporate critiques, not members at large of the public, that we do our due diligence and make sure the record reflects our vetting of the OEHHA response. I think we actually do that fairly well.

But I certainly wouldn't support us engaging in direct dialogue with people who submit those comments. Those are comments that would be -- on our record should reflect our scientific review of OEHHA's response. But that's our role. And it's something we should stick with.

CHAIRPERSON FROINES: I think we also have to be careful about the snowball rolling down the hill. And that is once you start letting people testify, there's no clear endpoint for what that is going to end up doing and it could end up taking enormous amounts of time.

I should say, I chaired the National Toxicology Program Committee on carcinogenesis. I would, as Chair, for example, I think we took up trichloroethylene and we had maybe consultants from industry. There may have been 15 -- 10 to 15. Well, it destroyed the scientific discussion of the Committee, because we felt like we were being hit over the head with a baseball bat with so many interested parties. And there was no science. The science fell by the wayside, because everybody started to get very defensive and reactive. And it was my experience

was that it really did have a profound effect on the success and failure of that Committee. And I just would hate to see that sort of thing happen again.

So I've seen the same thing with the Carcinogen Identification Committee when I Chaired it -- I didn't Chair it. I was on it. Again, the quality of the discussion has to be guarded I think so that we have the with -- the success of this Committee is the quality of the science. And we need to preserve that I think.

I'm sorry. I shouldn't have taken your --

PANEL MEMBER BUCKPITT: No. I can't add anything to that. I think you bring up a very valid point. This could get to be very quickly out of hand. I agree with Kathy that government needs to be open, but I think in the transcripts they can understand what is done in this Committee. They do have the opportunity to submit written comments.

CHAIRPERSON FROINES: So do we need to take a vote?

PANEL MEMBER HAMMOND: Let Beate speak.

PANEL MEMBER BLANC: Do you have anything to add, Beate?

PANEL MEMBER RITZ: No. I like written comments.

PANEL MEMBER BLANC: I would say that this discussion reflects consensus among the Panel as an

entirety that we do not wish to change the status quo. And we will not be receiving oral testimony.

PANEL MEMBER HAMMOND: And I'd like to add that we encourage people to participate in the workshops that OEHHA has, the public workshops, so there is a opportunity for public.

CHAIRPERSON FROINES: So it's sufficient not to take the vote, but take your words as the position of the Committee.

PANEL MEMBER BLANC: I think the transcript reflects there is unanimity of views, yes.

CHAIRPERSON FROINES: Thank you. That was a very good discussion of a potentially difficult issue.

PANEL MEMBER BLANC: Okay. Andy.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Well --

CHAIRPERSON FROINES: Thank you, Kathy, for spending more time than you had.

PANEL MEMBER BLANC: We'll tell you what he said.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I'll make this as brief as possible, obviously.

But yeah, I just wanted to say that the big thing which we're working on the moment is the official title is the Hot Spots Risk Assessment Guidance Manual, as it's

probably known as the Cookbook. And this essentially is a distillation of the risk assessment principles which are laid out in the technical support documents, which you as a Panel has reviewed starting with the non-cancer risk assessment TSD in 2008, the cancer risk assessment TSD in 2009, and the exposure and stochastic TSD, which you just approved a few months ago.

And the guidance manual is designed to distill this down into a practical user guide for people conducting the risk assessments. And it's parallel by a software application which is being written by the Air Resources Board staff which actually encapsulates the principles and ties it in with the air dispersion modeling software.

And so we are well on with preparing this document. We've actually just shared the draft of the cookbook with our co-authors over at ARB, and we are due to be sending it for review by CAPCOA, the air district's representatives, very shortly.

We are then going to be sending it out for public comment, and we're looking to present this for the Panel's approval. Now, Peter is going to be the one who discusses with you the timing. But we're talking about having this ready for your review in the early part of next year. And that would be our next objective to have this reviewed by

you.

It's important in a number of ways in that until this is complete, really, all the recommendations and technical support documents are very difficult for the Air Board and the districts to do anything with. So they really need this as the final piece to allow them to start implementing the recommendations which we've developed over the last several years.

It doesn't actually contain any new information, if you like. It's strictly based on what was in the approved TSDs. But at the same time, it's an important tool for getting those recommendations implemented. So that's our next big objective, which we will be bringing.

CHAIRPERSON FROINES: Can I ask you a question?

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Certainly.

CHAIRPERSON FROINES: Lauren Zeise was on the National Academy of Science Committee that published a document in 2009 Science and Decisions. You know that document?

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Uh-huh.

CHAIRPERSON FROINES: And that document is extraordinary, I think. It has -- it's very sophisticated, has very good science, and lots of good

recommendations in it.

Is there any connection between what you're thinking about now and that Science and Decisions document from 2009?

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I think some of the ideas which would explored by the NAS in 2009 were also explored by us in our technical support documents. I mean, the cookbook isn't about that depth of introspection or forward planning. But I think it's fair to say a number of the ideas which were raised in science and decision making, things like use of upstream endpoints and things like that, things like that are certainly ideas. I mean, they've been circulating in the risk assessment community at some level for a while prior to the NAS's final reports.

Of course, we did have the benefit of having Lauren Zeise around and talking to us during the time that we were developing the TSD. So I think it's fair to say that we're certainly not ignoring some of those principles.

It's also I think fair to say that the NAS report includes quite a lot of forward thinking. And I think it's clearly going to be incumbent on us to continue thinking about those principles. And in due course, we

may well find ourselves needing to add further to our risk assessment guidance to reflect new ideas as they are developed and make practical for use.

CHAIRPERSON FROINES: It's particularly important -- you realize it's quite a major change from the 1983 red book and that this document basically implies that risk assessment and risk management should not necessarily be kept separate, as has been the pattern in the United States for umpteen years. And so that the issue of risk assessment and risk management in the Science and Decisions document is something that I think everybody has to think about because it has implications for alternatives analysis, alternatives assessment, and for predictive toxicology and so on, so forth. So it's something that needs to be thought with some care, I think.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I think that's a good point. I think in defense of what we've been doing, I think it's fair to say that for some number of years, we've encapsulated in our process the idea that the risk assessment, risk management cycle is to some extent iterative, as you might say. This is why we've had the ideas of the different levels of complexity of risk assessment, which are in visage in the exposure and stochastic TSD.

It's also I think implied in the recent work which OEHHA and Melanie, in particular, are involved in of course in planning the handling of Green chemistry issues. So these are very much ideas which we are currently involved in and hopefully we'll be continuing to develop.

PANEL MEMBER BLANC: But on a practical matter, do you expect the revised butadiene document to come back to us also early in the year and therefore you would schedule a meeting that would be jointly dealing with both those agenda items?

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I'm assuming we will do that, although depending on your schedule and work loads, you know, that side of things is -- I'm not the person to address. But we could also do some work on the butadiene document by conference or something like that, if you preferred to do that. We're open to the options.

PANEL MEMBER BLANC: I would have said the opposite, if anything. It sounds like the document you're describing, if it came to us, could be done by a conference call and that the issues with the butadiene document were fairly substantive.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Well, we're amenable to handling it as you think fit. We'll follow the Chairman's direction on that.

But it is our hope that we can bring the cookbook to the Panel for review somewhat expeditiously, because there is a considerable amount of pent up energy for implementation waiting there.

So as I say, we'll follow your direction and see what is --

CHAIRPERSON FROINES: Peter was talking to me and I --

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: In terms of scheduling how and where and when exactly the review of that cookbook document comes up, we'll defer to what you decide and what arrangements can be made. But we're hoping it will be early next year.

Other things I'll mention just briefly on the horizon that we are working at the moment on reference exposure levels for benzene and carbon sulfide. And we are hoping to take these through the public comment workshop revision process and have them ready for presentation to you. But that would be -- in our sequence of events, that would be after we've finalized butadiene and the cookbook. So that was really -- that was the game plan which I wanted to lay out for you.

CHAIRPERSON FROINES: If we have RELS in -- we have numbers for benzene as a carcinogen, isn't that the defining number as opposed to the non-cancer effects?

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: To some extent, it depends on the exposure scenarios. And I think in this case, the non-cancer effects are -- or rather in the way that we have a mechanistic connection between the cancer and non-cancer effects in the butadiene case. I think you can say the same is true for benzene. The expected levels for the non-cancer effects are low enough that it may be necessary to consider those for certain exposure scenarios.

I can't make that prediction without having the final document in front of me. But I think the answer is, yes, it is an important aspect of benzene toxicity in particular.

CHAIRPERSON FROINES: I meant in general.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: In general, I think that if you are dealing with some of the carcinogens that we've produced numbers for that clearly the cancer number is going to dominate the risk assessment.

And this I think has been reflected in some of the TAC documents that that's been the focus because it was seen as the most important. What we're actually finding is that not withstanding the fact that those cancer numbers tend to dominate the long-term risk calculation, there are other important effects which

really ought to be -- we ought to be aware of. We ought to have a measure to make sure that we are not getting into a zone.

And I mean, I think, dare I say the things like the diesel assessment, we have more interest in some of the non-cancer effects perhaps as expressed in the concerns about various sorts of PM than we had initially just concentrating on the cancer effects.

So I think that the answer is yes, they're not always going to drive the risk assessment, but it's important to have an assessment and some sense of how these fit into the overall picture.

CHAIRPERSON FROINES: Do you have more?

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: No. Unless you want to ask me any further questions.

PANEL MEMBER BLANC: You don't have any knowledge about the Department of Pesticide Regulations, what they might be thinking about?

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I think my best answer to that question is to say no.

PANEL MEMBER BLANC: You're supposed to say, "Am I my brother's keeper?"

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT

CHIEF SALMON: Clearly not in that case.

CHAIRPERSON FROINES: Well, there is a Committee that's been established to look into the issues of agricultural substitutes and different modifications.

OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Of course, we -- or at least OEHHA does regularly hear from the pesticide people any time they are developing their assessments on the TAC program. Obviously, we are in communication with them and talk to them quite regularly. But they are the ones who take the formal lead on those issues.

CALEPA SECRETARY SOLOMMON: This is Gina Solomon man. I do have a little DPR update.

DPR is working on a document on chlorothalonil. And their intention, as I understand it, is to bring it before this Committee sometime in the late spring or thereabouts. So that's I think the next one the's coming your way from DPR.

There are some others that they're looking at after that, and so we're working with them on several pesticides in the pipeline.

PANEL MEMBER BLANC: I'd like to make a motion we adjourn.

CHAIRPERSON FROINES: Is there a second?

PANEL MEMBER NAZAROFF: I second the motion.

CHAIRPERSON FROINES: All those in favor?

(Aye.)

CHAIRPERSON FROINES: The meeting is adjourned.

(Thereupon the California Air Resources Board, Scientific Review Panel adjourned at 1:24 p.m.)

CERTIFICATE OF REPORTER

I, TIFFANY C. KRAFT, a Certified Shorthand Reporter of the State of California, and Registered Professional Reporter, do hereby certify:

That I am a disinterested person herein; that the foregoing California Air Resources Board, Scientific Review Panel meeting was reported in shorthand by me, James F. Peters, a Certified Shorthand Reporter of the State of California;

That the said proceedings was taken before me, in shorthand writing, and was thereafter transcribed, under my direction, by computer-assisted transcription.

I further certify that I am not of counsel or attorney for any of the parties to said hearing nor in any way interested in the outcome of said hearing.

IN WITNESS WHEREOF, I have hereunto set my hand this 30th day of October, 2012.

TIFFANY C. KRAFT, CSR, RPR
Certified Shorthand Reporter
License No. 12277