MEETING

OF THE

SCIENTIFIC REVIEW PANEL ON TOXIC AIR CONTAMINANTS

CALIFORNIA AIR RESOURCES BOARD

MILBERRY CONFERENCE CENTER

500 PARNASSUS AVENUE

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

SAN FRANCISCO, CALIFORNIA

FRIDAY, JUNE 15, 2001

9:30 A. M.

Reported by:
James Ramos

APPEARANCES

PANEL MEMBER PRESENT

Dr. John Froines, Chairperson
Dr. Paul D. Blanc
Dr. Anthony Fucaloro
Dr. Stanton Glantz
Dr. Hanspeter Witschi

REPRESENTING THE CALIFORNIA AIR RESOURCES BOARD

Mr. Jim Behrmann
Mr. Peter Mathews
Dr. Shankar Prasad
California Air Resources Board

REPRESENTING THE OFFICE OF ENVIRONMENTAL HAZARD ASSESSMENT

Dr. George V. Alexeeff
Deputy Director for Scientific Affairs

Dr. Melanie Marty
Supervising Toxicologist

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

Dr. Stanley Dawson
Air Toxicology and Epidemiology Section

Dr. Joseph P. Brown
Staff Toxicologist

Dr. James Collins
Staff Toxicologist

Dr. Judy Polakoff
Associate Toxicologist

Ms. Colleen Heck
Chief Counsel

Dr. Mark Miller
Public Health Medical Officer II

INDEX

PROCEEDINGS

CHAIRPERSON FROINES: We will officially call to order the Scientific Review Panel meeting for June 15th, 2001. We shall be discussing at the outset the issues surrounding SB 25, and why don't we proceed. And the first speaker, I believe, will be Dr. Melanie Marty.

SUPERVISING TOXICOLOGIST MARTY: Good morning. What we wanted to do was first go through some material on chemicals that came up at the last Panel Meeting as a concern to some of the Panel Members. Questions arose as to what information we found on those chemicals and why did we not think they rose to the top.

So, we can do that fairly quickly. We have four or so slides on each one, or I can just say it, however you want.

CHAIRPERSON FROINES: Show us the slides.

SUPERVISING TOXICOLOGIST MARTY: All right.

The first chemical is arsenic. Arsenic is a concern because of the toxicity information on arsenic. The epidemiology data are weak but suggestive of a possible differential toxicity between children and adults, and I'll go over that in just a second.

The airborne exposures are pretty low. The ambient air concentration ratio to our chronic REL is .03 or .04 or so. And our chronic REL also has an uncertain factor

of 1,000, so there's a certain amount of buffer room in that number.

There's some indication of differential effects in human studies on birth weight, fetal mortality, and congenital malformations, and this information comes from a series of studies done in Sweden near a smelter. The problem with the studies is that there's also huge exposures to lead. There's some exposures to cadmium and to mercury and there were no individual exposure measurements, -- but there basically is no exposure measurement.

There's also evidence of higher lung cancer in young men, and these are people aged 30 to 39 in a community in Chile that's exposed to concentrations of arsenic in drinking water that were pretty high, upwards of 600 micrograms per liter as kids and then the concentrations have dropped off because they've installed treatment. But, at any rate -- I think I have a slide on that actually.

And then there's some information from two studies, one in Thailand and Mexico, that there might be effects on intellectual development, but the problem with those studies again is they're fairly weak studies and lots of compounding, but it's a very intriguing finding and it could be that arsenic is impacting I.Q.

Then finally there's evidence of teratogenicity in animals, intraperitoneal exposure is relatively high. I'm

not sure of the relevance, at this point, to airborne exposures.

In terms of emissions to the air, in the air toxics hot spots program database for, I believe, it's reporting year 1999, there were about 11,000 pounds of arsenic emitted by facilities reporting to the program. And then the ambient air concentration was a little over a nanogram per cubic meter.

If you assume a certain breathing rate per day, you're getting about .02 micrograms per day from the ambient air. The major sources really are food and drinking water. And drinking water, the Department of Health Services estimates the average intake is about ten micrograms per day and for food, especially seafood, we're looking more at 50 micrograms per day. So the total exposure from -- airborne exposures are a pretty small part of the total.

Here's a little bit of information on the Ronnskar Smelter Studies and the effects they found. Significant reductions in birth weight; birth weight with parity, which is unusual, because usually the babies get bigger instead of smaller; significant increase in congenital malformations in one study, but the data were a little bit inconsistent; significant increases in, if you combined the spontaneous abortions and stillbirths, the study author called that perinatal mortality and found a significant increase, as you

get closer in to the facility.

So the communities that were closest to the facilities experienced these effects.

As I said earlier, no exposure assessment, and it was confounded by pretty high exposures to lead and other metals, so it's suggestive evidence, but it's on the weaker side.

And then here's Alan Smith's paper, looking at arsenic induced lung cancer, and this is exposures via drinking water in Chile, in a community in Chile, and you can see that the SMR for men age 30 to 39 is pretty large, 11.7 and the confidence interval goes from 6 to about 20. And the author himself expressed that he was concerned that the reason this age group had such higher lung cancer risk is because when they were younger than ten years old they were being exposed up to 570 micrograms per liter in their drinking water.

Because this is a fairly high exposure via drinking water it has somewhat limited relevance to what we're looking at now, although arsenic is definitely a lung carcinogen by the inhalation route, so it's actually pretty interesting.

And then here's a little bit of information on the two children's intelligence studies that I mentioned earlier. So they had actually in the one study in Mexico,

which is Calderon, et al, they looked at arsenic in the urine and found decreased verbal I.Q. with increasing arsenic in the urine. And they also found with increasing lead in blood they got decreases in certain of Wreshler Intelligence Scale Sequential Processing Tests.

And then the study in Thailand looked -- actually it was exposures in drinking water. It was surface water contaminated by a mine and they looked at hair concentrations and found that if the hair concentration was higher, the I.Q. of the child was lower and that arsenic exposure could explain about 14 percent of the variance in I.Q.

So there's definitely reason to be concerned about arsenic, but we just feel at this point that the airborne exposures are such a small part of the total that it doesn't really make it to the top five.

PANEL MEMBER BLANC: Two questions, just to generalize from this. One would be from a policy point of view what would be the proportion of air to total body burden that would make you --

SUPERVISING TOXICOLOGIST MARTY: Be more worried?

PANEL MEMBER BLANC: Be more worried or wouldn't raise the bar? In other words, I don't think any of us would require that it be 51 percent, you know, that you'd have to show that the majority of the exposure were from

air, but would it be ten percent or five percent?

DEPUTY DIRECTOR ALEXEEFF: Well, it would probably be a health effect, but pretty much 20 percent would definitely be an issue. In other programs where we're looking at relative source contributions, when things are at 20 percent, it would be a concern. But it's not a bright line, but 20 percent definitely.

PANEL MEMBER BLANC: So there would probably be the sense that something less than one percent wouldn't come in, something 20 percent or more would definitely hit the bar. And if you were talking about something that was between five and 20 it would be a subject of some discussion, is that a reasonable --

SUPERVISING TOXICOLOGIST MARTY: Yeah, a fair analysis.

PANEL MEMBER BLANC: My second question or more of a comment would be that one of the suggestions that I made to Dr. Froines and I think is reflected in this draft material is that there are really two different issues that we're looking at here.

One is the evidence that a substance has a differential effect in children. And I think to evaluate the scientific evidence in that regard we can adapt, roughly speaking, Bradford-Hill criteria so that we can look at the strength of the association, the reproducibility of it, the

biological plausibility, in particular which has been an issue with some of the associations.

And then there's a second sort of column of issues which has to do with how much exposure is there and how much public health policy implications is there to the exposure. In other words an exposure may, in fact, be present, but if there's no conceivable public policy that's going to intervene or, looking the other way, if there's already a lot of policies in that regard, it may not rise to the threshold on that account.

So coming at arsenic from that point of view, the issue with arsenic is not that the biological evidence isn't plausible and it's not that there -- there could be more studies, but there's certainly been enough to raise a fair amount of concern, but, in fact, exposure, the current exposure levels do not appear to meet the threshold for public action. Is that a fair summary?

SUPERVISING TOXICOLOGIST MARTY: The current airborne exposures, yes, I think that's a fair summary.

PANEL MEMBER BLANC: And do you think that that's an approach that we can take as we go through these other presentations that you make and some of the written documents as well?

SUPERVISING TOXICOLOGIST MARTY: Yes.

CHAIRPERSON FROINES: I think that this approach

that Paul has just enunciated I certainly agree with and I want to make sure that the rest of the Panel feels comfortable with what he's suggested. So, Peter, Stan, Tony?

PANEL MEMBER GLANTZ: I generally agree. My only slight quibble is, I think that a couple of the things that you said near the end sort of really spill over into regulatory questions, which really we shouldn't be addressing, I don't think. We should just be looking at the scientific evidence about is there evidence that there's particular reason for concern for these compounds regarding children. And maybe I misunderstood what you were saying near the end, but --

CHAIRPERSON FROINES: I think I would subdivide Paul's comments and he can disagree. One is the question of is there sufficient exposure in California to consider it a matter of concern, and I don't think that falls into a risk management.

I think the question of whether or not if something is already under a control strategy plan, maybe crossing the line to some extent and I would certainly weight that much less so that we don't into an area that is really out of our statutory definition.

Do you agree with that?

PANEL MEMBER BLANC: Yeah, I was just thinking,

for example, an example might be, you know, we actually can't look at pesticides, but let's suppose we were allowed to look at pesticides and we had data on DDT and its metabolites in terms of their preferential effects on children. I mean there's still a lot of residual DDT in breakdown products in the environment, but it's already a banned substance.

You know, what would be the utility of raising it up to -- so in that point of view, I think what I'm getting at isn't a regulatory issue so much as taking into account, not only what the current exposure levels are, but what the trajectory of those exposure levels is going to be absent any further intervention.

And I think that that, for example, that's quite important when we come to manganese where the current exposure levels are very low.

CHAIRPERSON FROINES: We certainly are within this law or rather OEHHA is precluded within the law to address pesticides. That doesn't mean that in our findings we can't make a comment about our views on the fact that pesticides are excluded. So we can come back to that at a later time.

Melanie, -- and so I think the bottom line, based on this discussion is that given the level of evidence and the level of exposure that you would recommend that arsenic be considered as a quote, "Tier 2" compound, and if that's

the case then we should move on to the next --

SUPERVISING TOXICOLOGIST MARTY: That's the case. I would not put it in Tier 1 at this point.

The next chemical is carbon disulfide. Carbon disulfide, there is some evidence of increased sensitivity to acutely lethal exposures and also evidence of lower metabolic rates in new born animals.

There is some evidence, although it might be called equivocal of teratogenicity in rodents. It's definitely a neurotoxin in adults, as seen by occupational exposures. Neurotoxicity is an endpoint which we identified as important to children but we have little to no evidence of differential effects for neurotoxicity.

And finally there's really a fairly low potential for exposure in California. We have no ambient concentration data for carbon disulfide, but in the air toxics hot spots program database, California industry has reported about 1800 pounds of CS2 emissions in 1999.

Interestingly enough when you look at the federal database, the toxics release inventory database, from three refineries we actually got more than they reported to the Air Resources Board, so we're going to have to look into that.

The Air Board looked for us at the ATEDS database to see where the CS2 was coming from. It's primarily a

fugitive emission from refineries and it looks like the sulphur recovery units would be where it was coming from mostly.

In terms of toxicity studies for acute exposures, one-day old rats were about three times more susceptible than 20 to 40-day old rats to lethality. This was an LD 50 study.

Also in a metabolism study by Synderwine and Hunter 40-day old rats metabolized more CS2 to carbon dioxide and expired less CS2 via inhalation than one-day old rats.

And in terms of developmental toxicity, rabbits inhaling CS2 at gestation days six through eight showed developmental toxicity at 600 ppm, with little maternal toxicity at that dose level. So that is an evidence of some differential sensitivity.

There were also other developmental toxicity studies. Some of them found -- they found different types of effects at different doses, including reduced fetal body weight and post-natal growth.

The transient delays in development were found at 3 ppm in rats in the Tabacova and Balavaeva study, but nobody else seemed to report that.

Also in the two-generation rat study there were terata reported at 3 ppm, but only in the second generation

and not in the first generation, even though they were also being exposed.

And basically growth retardation perinatal mortality embryo and fetal survival were the types of things that were decreased by quite different ranges of exposures.

Some of the studies found terata at high concentrations and some of them did not.

And there's just a few studies that kind of indicate that maybe there's a differential sensitivity, but maybe not, so in other words, the concentrations that resulted in significant, either fetal toxicity or, in this case, unossified sternebrae, which is basically a developmental delay, also were very toxic to the mothers, and that's just the point of this slide.

So, we do when we look at developmental toxicity, we do consider whether the doses were maternally toxic or not and you tend to weight it less if the doses were maternally toxic. But overall I think you could say that there's developmental toxicity associated with carbon disulfide.

And this again, the issue that's keeping it out of Tier 1 is exposure. We just don't think there's a lot of exposure to CS2. We would encourage the Air Board to look into the TRI database and figure out why those facilities reported different amounts to the feds than they did to the

states. And it would be very nice if we could get some actual measurements of CS2 near facilities, but at this point I don't think we can put it into Tier 1.

CHAIRPERSON FROINES: But I also heard you suggesting that the data was somewhat equivocal?

SUPERVISING TOXICOLOGIST MARTY: The reason I said that is because in certain studies that used fairly high concentrations they found no developmental effects. In other studies with quite lower concentrations, they did find developmental effects. They weren't necessarily looking at the same endpoints, so that's a little bit of an issue.

But there's so many studies that did find something, either reduced growth delays, reduced body weight, developmental delays, that I think you can say that's pretty strongly suggestive evidence that CS2 can cause developmental toxicity. So it's still an important chemical.

PANEL MEMBER BLANC: And also I think it's one of the few chemicals we've had presented to us where there really are convincing metabolic data that newborns metabolize the toxin more slowly and therefore the half life is longer. Would you agree with that?

SUPERVISING TOXICOLOGIST MARTY: Yes.

PANEL MEMBER BLANC: And one of the end points that is also an issue with this toxin is that in addition to

neurotoxicology is athrosclorosis, and I think that would also be a concern if you had children exposed, starting at a young age, in terms of -- in the same generic sense, you know, that cancer has been an issue to your --

SUPERVISING TOXICOLOGIST MARTY: Okay. I should have mentioned that, Stan, I'm sorry, within occupational studies, athrosclorosis has been associated with CS2.

PANEL MEMBER GLANTZ: I don't like nagging, but cancer is not -- I think there's evidence of environmental causes of heart disease too, which has gotten very little attention from anybody.

PANEL MEMBER BLANC: Do you know whether there's any information or has there ever been any monitoring near geothermal sites, because that would be another area where you would expect natural release of this potentially. Volanic sources are one of the few natural sources.

SUPERVISING TOXICOLOGIST MARTY: We can check that out, ask the ARB if they have ever looked at that. Certainly there is reduced sulphur monitoring near geothermal sites, but I don't know if they've ever --

PANEL MEMBER FUCALORO: Do you have any idea what the lifetime of CS2 in the atmosphere is?

SUPERVISING TOXICOLOGIST MARTY: I don't.

CHAIRPERSON FROINES: I bet it's longer than we think, but that's a guess.

PANEL MEMBER FUCALORO: I don't know what I think, so I'm --

(Laughter.)

CHAIRPERSON FROINES: Melanie, I think that it would be -- I don't know, have there been any studies, as far as you know, of measurement of carbon disulfide in and around petroleum refineries, because we certainly have a lot of sulphur to worry about within that environment.

SUPERVISING TOXICOLOGIST MARTY: I'm not aware of any, I hate to say I'm not aware of any, but if anybody is here from the Air Board who could answer that question?

CHAIRPERSON FROINES: Is there?

DR. PRASAD: It's been correctly planned and in the Bay Area there'll be two sites which we'll be monitoring for carbon disulfide starting in the next couple of months.

Shankar Prasad from the Air Resources Board.

CHAIRPERSON FROINES: I think this is an important point. I think that there is sufficient evidence to indicate, as we've known for quite some time about the toxicity of carbon disulfide, so if there is a potential for hot spots I think it's worth documenting. And so we'll presumably proceed with this is a Tier 2 chemical from the standpoint of SB 25, but I think it's a general issue as a toxic air contaminant that it is something for which we should have additional information on potential exposures in

this state. Especially because it really does affect so many different end points, toxicologically.

PANEL MEMBER BLANC: Well, also, John, wasn't it one of the minor breakdown products of metam sodium?

SUPERVISING TOXICOLOGIST MARTY: Yes.

PANEL MEMBER BLANC: And that is the -- well, we'll come back to this one-page summary issue, but I think it's --

CHAIRPERSON FROINES: And my impression from that, Paul just said of the minor breakdown products of metam sodium, but I suspect that we really don't know, either as a biotransformation product or as an atmospheric breakdown product to what degree carbon disulfide is produced relative to some of the other compounds.

Let's go ahead. We're going to have to avoid these kind -- I just fell into talking about a subject area that I'm interested in and I know Paul is interested in it too, and we're going to have to be careful today to avoid some of that so we stay on some sort of reasonable timeframe.

SUPERVISING TOXICOLOGIST MARTY: Another chemical that came up at the last meeting was chlorine, which, as everyone is aware, causes irritation of the respiratory tract, eyes and skin. As such you may suspect that chlorine might exacerbate asthma, and OEHHA has identified asthma as

a disease that disproportionately impacts children, thus children may be more susceptible to chlorine in the air.

A study by D'Alessandro, et al, of which Dr. Blanc was one of the authors, did demonstrate in adults who were hyper-responsive that they showed a greater loss in FEV1 and a greater increase in airway resistance than five normal adults at 1 ppm. And I'm recalling correctly that at .4 ppm the difference was not significant between the hyper-responsives and the "normals".

We did try to look at any information from accidental releases, because chlorine is probably number 2, if I'm recollecting correctly, in terms of accidental releases, ammonia being the first.

There was one study that we found on accidental release of chlorine vapor at a swimming pool in Italy and there were quite a number of kids and adults present who experienced respiratory symptoms and it seemed that about the same percentage of adults and kids experienced respiratory symptoms, for whatever that's worth. And that more adults reported persistent respiratory symptoms after the accident than kids. A little bit of information, I don't know if you can do too much with that.

The emissions information that we have from ARB's ATEDS database in '99 indicated considerable emissions statewide of chlorine, 245,000 pounds or so. In talking

with the chemists at ARB, chlorine levels are not routinely monitored in California because it's too reactive and they can't measure it.

They do measure chloride in particulate, so on their website chloride as particulate is reported, but it's not chlorine gas, it's largely soluble salts of chlorine -- chloride salts.

PANEL MEMBER GLANTZ: And the emissions are due to what, primarily?

SUPERVISING TOXICOLOGIST MARTY: That I would have to ask ARB to respond to. I don't know myself.

PANEL MEMBER GLANTZ: Hypochloride?

SUPERVISING TOXICOLOGIST MARTY: No, this is actually chlorine gas emissions.

PANEL MEMBER GLANTZ: Yeah, but hypochloride will go to chlorine.

SUPERVISING TOXICOLOGIST MARTY: Oh, hypochloride, I'm sorry.

PANEL MEMBER BLANC: The issues include that we do actually have hypochloride manufacturing here but also chlorine is a major intermediate in chlorinated hydrocarbon manufacturing. So I'm assuming it's largely in the petrochemical industry one way or the other. It's not refining, per se, it's synthesis.

I don't know if we have primary chlorine gas

manufacturing facilities in California or not, to tell you the truth.

CHAIRPERSON FROINES: We really don't have much petrochemical manufacturing either.

PANEL MEMBER BLANC: Well, this would be, you know, breaking it down, you know, -- and that I don't know. But the reason why this number underestimates is that what it won't include is the small point source releases, including water purification plants, swimming pools and then household releases. But the issue in your chlorine presentation, as opposed to the last two, is not that you don't think the exposure potential is widespread, it's really more that the database for preferential child effect is very weak.

SUPERVISING TOXICOLOGIST MARTY: It's limited.

PANEL MEMBER BLANC: And it would rest entirely on two suppositions. One is that one could reproduce the findings that people with airway hyper-responsiveness are preferentially responsive. And the extrapolation that was made earlier that, ergo, children, because they have smaller airways and have more asthma would bear the brunt of this.

So, to the extent that you would show that people there with hyper-responsiveness respond preferentially, if that were established then, based on the criteria you've set forth in the document, you'd actually be forced to put it in

tier 1, because you've already stated that that's going to weight heavily. But I don't think that the database supports that preferential response in airway hyperactivity.

SUPERVISING TOXICOLOGIST MARTY: Yeah, I would agree to an extent, but I also don't think that there's widespread exposure to chlorine, except what is not widespread. Accidental releases are really the issue.

PANEL MEMBER BLANC: Yeah, but they're a common enough event, I think, that we're talking about something of concern, particularly these little small point source exposure --

PANEL MEMBER FUCALORO: They're not accidental, they're just released. I mean if you want to call it accidental, but they are --

PANEL MEMBER BLANC: Unintended.

CHAIRPERSON FROINES: But I also think, I don't entirely agree with Melanie. I think that what you say may be true, but it also, given the level of this discussion, it suggests that we don't know either.

SUPERVISING TOXICOLOGIST MARTY: The water treatment plants, the big ones are already in the hot spots database, but there's probably little ones all over the place that aren't. That's another problem.

CHAIRPERSON FROINES: There's a lot of swimming pools in southern California. But I think that the other

point to make is I think Paul is trying to press on your defining as clearly as possible the basis of your decision-making.

SUPERVISING TOXICOLOGIST MARTY: Yes.

The next chemical that came up at the last meeting is manganese. Manganese is definitely neurotoxic and animal studies are out there which show that rat pups, rodent pups are more sensitive than adults. However, the ambient air concentrations and the potential exposures appear to be relatively low.

The other issue is that manganese is actually an essential nutrient and that exposure from your diet is about four orders of magnitude higher than from typical ambient air, which we'll get to in a second.

Manganese is an essential nutrient. It's needed for lipid-synthesis and oxidative phosphorylation. There's actually an adequate daily intake set for kids, one to three, of 1.2 milligrams per day. And then for men and women between about two milligrams per day.

There have been a couple of studies, looking at kids who were hyperactive and/or learning disabled, both, I guess. And they looked at elevated hair manganese levels as -- or they looked at hair manganese levels as an indicator of exposure to manganese. And in this study the children who were learning disabled had higher levels than normal

kids and the difference was significant at $p<0.05$.

However, no correction was made for compounding for other exposures, including lead.

There have been some indications that pediatric patients on Total Parenteral Nutrition are more likely to show neurotoxic effects of manganese than are adult patients, so there's three or so citations looking at that issue.

In terms of the experimental animal studies, young rats showed neuronal degeneration in the cerebral cortex and cerebellar cortex after only 30 days of oral administration of 50 micrograms of manganese per day -- manganese chloride per day.

Adult rats required a longer time period to show the same amount of neuronal degeneration, so that right there is an indication that young animals are going to be more sensitive to manganese neurotoxicity.

There's some information, and I don't know what to do with this, but that manganese homeostasis is suspended during pregnancy and lactation from farm and lab animals. We're not sure if that is the case with people. And the suspension of the homeostasis allows for higher levels of manganese in fetal and neonatal blood and tissues.

So if you're being exposed young to elevated manganese, you're in trouble from a homeostasis standpoint.

Studies have been done looking at rat pups exposed as neonates to manganese and it's showing that there's elevated brain levels of manganese relative to the control, so it's getting into the brain.

PANEL MEMBER FUCALORO: And this is all manganese 2, right, manganese plus 2?

SUPERVISING TOXICOLOGIST MARTY: Yes, that's right.

And adults only showed increased brain levels, but the exposures had to be higher, so that again is an indication that pups are going to be more sensitive to impacts on the brain.

And also there have been some neurobehavioral studies, looking at hyperactivity in rat pups at post natal day 21 who were exposed as neonates to manganese in their drinking water. They also, Pappas, et al, '97, observed basically the same thing, increased locomotion and rearing in an open field in rat pups whose mothers were exposed during gestation. So this is gestational exposure resulting in hyperactivity in the offspring.

And then also, following oral exposure as neonates, at post natal day 21, the animals exhibited increased acoustic startle response, which is along the same lines as a hyperactive animal would -- you would see in a hyperactive animal.

In terms of actually looking at histological evidence, cortical thinning has been observed in rat pups who were exposed -- whose mothers were exposed, so this was in uter exposure looking at the rat pups post natal day 32 and observing cortical thinning in the brain. There was some comment by the author that it may result -- maybe it was not just manganese, but have something to do with the nutritional status of the animals. And then Dorman, et al in 2000 did not see this neuroanatomical effect.

And then again some evidence of lack of manganese homeostasis in newborns. Newborn mice are unable to excrete manganese very well relative to an adult mouse and maintain manganese blood levels relative to an adult mouse for the first 17 days or so of life in this study. And then, interestingly enough, manganese in the hair of human infants has increased significantly during the first six weeks after birth if you're formula-fed, but not breast-fed. And formula has a lot more manganese, especially formula made with soy, than breast milk.

In terms of exposure considerations the ambient levels of manganese are fairly low as measured by ARB's monitoring network. There are some significant hotspots emissions, 105,000 pounds per year statewide in '98.

The daily exposure from the diet for a child should be about a milligram per day. If you use the ambient

concentration measurements, then from ambient air they would be getting about 210 nanograms. Now that's average ambient, it's not next to a hotspot, so we still have some concerns about the hotspots emissions and unfortunately we don't have information on what concentrations are found near source.

PANEL MEMBER FUCALORO: And what are the sources for emissions of manganese?

SUPERVISING TOXICOLOGIST MARTY: This is a good question, if anyone from the Air Board can help me out on it?

PANEL MEMBER FUCALORO: I guess what I'm asking is all these data, toxicological studies are based on manganese plus two.

SUPERVISING TOXICOLOGIST MARTY: Uh-huh, so what is --

PANEL MEMBER FUCALORO: It's quite possible it's a higher oxidation state of manganese --

SUPERVISING TOXICOLOGIST MARTY: Okay, I can tell you that the --

PANEL MEMBER FUCALORO: It's particulate matter I assume?

SUPERVISING TOXICOLOGIST MARTY: Yes.

I can tell you that manganese is reported as total manganese and it's not speciated.

PANEL MEMBER FUCALORO: I understand, depending on

how they do the analysis. I mean, they can do total manganese. But, you know, chromium, I mean not to say that this is as bad as chromium, but chromium 3 or chromium 2 is not very toxic, but it's chromium 6 which is the hexavalent state of chromium, which is, and that's the one that's of great concern.

And so I'm just wondering if there's similar -- I'm not a toxicologist, I'm just wondering if there's a similar situation with manganese?

PANEL MEMBER BLANC: I don't think the toxicological data has suggested that. And some of these experiments are done with manganese chloride and some are done with manganese oxide and, in fact, organo-manganese compounds seem to have quite a bit of neurotoxicity as well.

There is another issue in terms of the relative contribution of inhalation versus ingestion and that is that the -- well, there's two issues. One is that the absorption from the respiratory tract is probably far greater than from ingestion. There's a lot of data that suggests that and, in fact, the most severe intoxications are from inhalational exposures in occupational groups.

And the second issue is that there's even some more recent intriguing data that suggests that it may not be the respiratory fraction, but that in animal models manganese deposited in the nasal tract is actually taken up

directly by neurons in the olfactory tract and transported directly to deep brain centers and that may be, in fact, the route of exposure that matters the most for some of the basal gangliar effects of manganese.

So the issue here that people get more from their diet and that you have a minimum dietary requirement may not be applicable as the science changes. It's a very unusual scientific issue, but nonetheless, I think it's one that should be recognized.

So, in summary, in terms of manganese, my impression from your presentation would be that the preferential effects on children is as strong for this substance as for any that we've looked at virtually, absent maybe lead.

SUPERVISING TOXICOLOGIST MARTY: Lead or mercury I think really are up there. But, yes, definitely --

PANEL MEMBER BLANC: Okay. And therefore the sole issue is the levels of exposure, either current or projected. And that being said, I think that both in our findings and certainly in your final report, I think there needs to be some very strong wording that if this is to remain -- that this may be tentatively put in tier 2 to start with, but here are the areas in which there's, you know, very high levels of concern if either the hotspots data reveal a population at risk within discreet

geographical areas or if there is introduction into California under any circumstances of new sources of either inorganic or organic manganese exposure.

CHAIRPERSON FROINES: I'd like to follow up on that.

As I sat and listened to the presentation, my sense is that up to now we've talked about there being two tiers, and when you originally presented your information you had the 11 compounds, five in the first tier, six in the second. I would almost argue that one should further subdivide the approach and actually have three tiers, because I think that manganese is considerably different than arsenic, for example.

I think arsenic is a very very important compound from the standpoint of carcinogenesis, for example, but in terms of children's effects it doesn't rise to the same level. Whereas manganese, the evidence seems quite strong relatively speaking, and in that regard when we have -- you know, this law forces us to make decisions based on very limited evidence and that's one of the difficulties and the frustrations about the SB 25 process, that the evidence is so limited. And where we do find sufficient evidence, then it seems to me we have to highlight it and take it quite seriously.

And in that respect I would argue that we put

manganese in its own tier and there may be other things that join it, but at least at this point that it doesn't just get lumped with vinyl chloride and glycol ethers and noncoplanar, PCBs and arsenic and chlorine.

PANEL MEMBER GLANTZ: Can I argue against that?

CHAIRPERSON FROINES: Let me just finish my point.

The 105,000 pounds per year is obviously -- I agree, by the way, with Paul, I think that the weakness of the argument that you make here is that the toxico-kinetics are not effectively taken into consideration and that's unfortunate, but let's let it go for the time being. We all recognize that there may be a significant difference between the uptake through the gut and through the lung or through the nasal passages as Paul suggested.

But I always have problems when we look at these ambient air exposures for California because I live in Los Angeles and we have more of everything.

(Laughter.)

CHAIRPERSON FROINES: And in that regard, to compare Mt. Shasta with, you know, Pico Rivera, just is not -- it's apples and oranges. And so when you tell me about hotspots and manganese I worry that there are places where the concentrations are considerably higher.

So this is actually a substance that I think requires real follow-up activity. And it needs to be

pinpointed, especially given its potential for long-term use on a national basis as well, and I don't think we should take that up here.

But I think that we need to further clarify the exposure question and I personally -- Stan's about to occur argument notwithstanding, would put some emphasis on manganese in at least our findings.

PANEL MEMBER GLANTZ: Well, I don't have any problem with putting emphasis on manganese in the findings and including the points that you two have made. But I think, you know, if you go back to what you said earlier about SB 25 has required us to move this process quite quickly and not dig into certain things with the level of compulsiveness that we've sometimes done, I think to then start subdividing the second tier even further is just silly, and I think it will open us up to further criticism.

I mean I think -- and remember we have a couple of more tiers we're not even talking about which are those long lists in the back of the document. And so I really think we should do as we have in the draft findings that I worked with Melanie on, which are, before we discuss, I need to explain how they're structured. They're a little unusual.

But I think we should say these are the five and these are the remaining, however many there are, and it doesn't have to be six, it can be however many there are,

with why we think that they're important. And I think that to include the kind of statements that you've been making in the findings is totally reasonable and appropriate.

But I just think to start subdividing that list further is just silly and I think that the points have been made, I think they're on the record. This is going to be an ongoing process and I think they'll be taken into account, and if they're not then at that point we can jump up and down. But I think that it's just not appropriate to start subdividing that and prioritizing within the -- you know, we've got the top five. We've got the bottom whole bunch of them and then we're talking about this intermediate list which isn't going to be that long a list anyway. And I just think if we put manganese in there and we say the things that have been said that that's adequate.

PANEL MEMBER FUCALORO: But you know, I'm agnostic on this issue, but I think Paul's mission has been that we mention the reason why a particular substance that makes for tier 1 and they fall into two categories, possible categories, differential toxicity and the other is exposure. And I think that would be sufficient that we make sure that those two points are made for every substance that doesn't make the list.

PANEL MEMBER GLANTZ: I don't have a problem with that.

CHAIRPERSON FROINES: Okay, why don't we come back to this. I probably was premature. I think that we should take this up when we talk about our findings. This is one where I think there should be some level of emphasis that's different than some other compounds, but I think we can take that up when we get there. And we'll ask Stan to make an argument that's different than this is silly. We'll go for the more substantive argument at that point.

(Laughter.)

PANEL MEMBER GLANTZ: I thought that was a pretty substantive argument.

CHAIRPERSON FROINES: Go ahead, Melanie.

SUPERVISING TOXICOLOGIST MARTY: Okay.

The fifth chemical that came up at the last meeting is methyl bromide. There is some -- and I have to say that this is a pesticide, but that regulation of methyl bromide as an emission from a stack from fumigation chambers has been allowed by a court decision.

There is some evidence of teratogenicity in reduced birth weight in rabbits and rats. Methyl bromide is a neurotoxican. It's been observed many times in occupational settings and following accidental exposures and also in animal studies. And neurotoxicity is an end point of concern for infants and children. But exposures to methyl bromide are not widespread from stationary sources.

Methyl bromide is neurotoxic. Occupational exposures have resulted in neurotoxicity. I just put a few of the references that are available in the literature going all the way back to the 1940s.

Animal studies have repeatedly demonstrated neurotoxicity. Rodents seem to be somewhat resistant, but dogs are a sensitive species. And the symptoms noted in both people and also in animals include headache, nausea in people and vomiting, tremors, convulsions and other signs of neurotoxicity in animal studies.

In terms of differential effects, we don't have any studies of neurotoxicity in neonates or young animals versus older animals, but neurotoxicity is definitely an end point of concern for kids because their nervous system is developing all the way throughout lessens. Developmental effects have been noted in rabbits at 80 parts per million, including gall bladder agenesis which was repeated in another study by Breslin. It's very unusual to not see any historical controls to any extent.

Also reduced birthweight and fused sternebrae are noted in the rabbit study by Breslin.

Rats have also showed reduced body weight gain in pups exposed during lactation, so this is a young animal exposure showing an effect. And exposure of rats in utero has resulted in decreased brain weight and this was noted at

30 parts per million by Norris, et al and also in the width of the cerebral cortex, which was noted at a higher dose in two other studies.

So I think the upshot is we know it's a neurotoxicant. We can see effects when exposure occurs in utero. We are somewhat constrained in looking at exposure issues since we only can consider basically fumigation chambers and exposures from fumigation chambers. We know there's some emissions from fumigation chambers in ports where they're using methyl bromide to fumigate fruit that comes in from out of the country.

CHAIRPERSON FROINES: With hexane, 2, 5-hexadione you argued that there was no evidence of differential toxicity and that the distal axonapathy that occurs does not appear to be an age related or a children related phenomenon. But here you just have made the statement that said it's neurotoxic and children have developing brains, therefore there's a matter of concern.

And there's a little contradiction between -- on the one hand you're saying that because of developing brains, neurotoxicity is a potential problem and in one case you say methyl bromide, that that may be an issue and with hexane you say it isn't an issue. So I think that one has to be careful in discussing the evidence to suggest that is there a mechanistic basis that the developing brain may be

more particularly susceptible to the mechanism of a particular neurotoxicity. And that's just a general comment.

PANEL MEMBER BLANC: Well, I think the big -- you know from a theoretical point of view, because this is an issue of central nervous system, toxicity versus peripheral nervous toxicity, that may be the rationale. But, in general, if you had to characterize, leaving aside the fact that the exposure levels appear to be quite low from the source that you can look at, that the database on a differential effect is modest, at best.

SUPERVISING TOXICOLOGIST MARTY: Yes.

PANEL MEMBER BLANC: And certainly there is no evidence in the key end point which would originally raise the material concern, which is neurotoxicity specifically. So I think that needs to be clear in your summary and I think we'll make it clear in ours if this is one of the ones which is weak on two fronts.

Up until now you've actually presented a series of chemicals which have one thing missing, but are strong on one or the other, whereas this is actually weak on both.

PANEL MEMBER FUCALORO: Are you suggesting a third tier?

(Laughter.)

PANEL MEMBER BLANC: No, no, I'm just saying that

of all the ones we've heard so far, I mean I think there are others in tier 2 which are also weak on both counts. But, again, I'm just saying that this -- again, I'm trying to return to the systematic way of looking at the data you're presenting.

The only other way in which one could indirectly look at methyl bromide I think would be by trying to look at the literature on differential effects of bromine -- not bromine gas, but bromide, I should say. And I wonder whether or not you did that, because, you know, one of the thoughts about methyl bromide is that it just happens to be a very effective delivery mechanism for bromide to the CNS.

SUPERVISING TOXICOLOGIST MARTY: I don't know how much staff looked at that. I do know that there was one paper that we pulled that indicated, and I'm remembering it was an in vitro system that methyl bromide was more potent than the equivalent amount of bromide ion in the system, and it was an in vitro nervous tissue --

PANEL MEMBER BLANC: Right, but I was asking a different question, which would be just bromide exposure of neonates versus adults, a propos, bromism, and that would be a very indirect argument, but I think it wouldn't be irrelevant to the issue. And I only bring it up because your data are otherwise so -- there aren't any other data that suggest any differential neurotoxicity.

I'm actually not aware of -- you know, bromism, historically, was an illness in adults, not in children, for medication sources.

CHAIRPERSON FROINES: Just two quick questions.

One, just a rejoinder to Paul, CPDA is not simply peripheral it's also central. So I think one can't just simply think of hexane as a peripheral, even though that's obviously the manifestation that's most commonly reported.

Secondly, the -- are you familiar with any studies of DNA methylation with respect to methyl bromide?

SUPERVISING TOXICOLOGIST MARTY: Only the genotox studies that have been done and it's a bazaar compound because it's genotoxic in several assays, but nobody can seem to get tumors in the carcinogenicity studies.

PANEL MEMBER FUCALORO: Go ahead.

SUPERVISING TOXICOLOGIST MARTY: The sixth chemical that came up is methylene chloride and the reason for concern is that methylene chloride is metabolized to carbon monoxide and that people poisoned by methylene chloride have elevated levels of carboxyhemoglobin.

We also have concerns about hotspots releases and therefore potential near source exposures. However, if you look at the ambient data, which has been collected by the Air Resources Board monitoring network, the measurements are very low. Our chronic reference exposure level is based on

the formation of carboxyhemoglobin in adults and if you ratio the ambient air concentrations to our chronic REL, the ratio is .005. So we're pretty far away from our chronic REL, which does have an uncertainty factor built into it for intra-human variability.

CHAIRPERSON FROINES: Are there hotspots measurements?

SUPERVISING TOXICOLOGIST MARTY: There are lots of emissions. It's in the millions of pounds per year, but we don't have any indications of what the concentrations are around most of those facilities. We have a few facilities that reported some years back and did a risk assessment, and methylene chloride did not drive -- it was a cancer risk at the time that was being looked at, so it's kind of hard to tell by looking at those numbers.

CHAIRPERSON FROINES: I think looking at methylene chloride from the standpoint of ambient concentrations may not be the best way to do it, because, you know, there's a million furniture refinishing shops that use methylene chloride as a paint removal aid, stripper. So that probably the problem is more localized, rather than general.

Go ahead, sorry.

SUPERVISING TOXICOLOGIST MARTY: We know that lowered birth weights in humans have been associated with prenatal exposure to carbon monoxide.

We also know from an animal study that prenatal exposure to methylene chloride can cause slower behavioral adaptation in pups at ten and fifteen days and altered activity levels in adulthood. So that's a prenatal exposure that produces an effect. It's fairly high concentrations.

We also looked at a study, Anders and Sunram, that evaluated the carboxyhemoglobin levels in the animals at maternal exposures to 500 or so ppm of methylene chloride and they got equivalent carboxyhemoglobin levels in the rat fetuses if the moms were exposed to 22 ppm or to 500 -- 22 ppm carbon monoxide or to 500 ppm methylene chloride.

This slide basically just says that in a picture that the equivalent carboxyhemoglobin levels are produced in the fetal tissues with 22 ppm CO and 500 ppm methylene chloride on the left. And then on the right are measured -- I think these are maximum measured levels of both CO and methylene chloride in 1999 and you can see that the max for CO was 23 ppm and the max for methylene chloride was 4.8 parts per billion.

So in terms of the overall contribution to carboxyhemoglobin that we might get from ambient levels of methylene chloride, it's pretty tiny compared to carbon monoxide.

CARB has one analysis where they looked at the statewide median in maximal monitored ambient methylene

chloride levels and I think this is 2000 data, it was .5 was the median and 4.8 was the maximum measurement. So the median levels are actually quite a bit lower than that one max, another order of magnitude down.

But we do have information that 8,000 tons or so were released in 2000 and that's actually up from the data that we had in '98.

PANEL MEMBER BLANC: That's not the hotspots -- or that is the hotspots data?

SUPERVISING TOXICOLOGIST MARTY: Yes, it's the hotspots data. It's tons per year.

And then, of course, the chronic REL, just for reference is 100 ppb. So compared to ambient we're pretty -- we're down there.

CHAIRPERSON FROINES: Do you know what the levels were in Mates II?

SUPERVISING TOXICOLOGIST MARTY: In the Mates II study, I don't remember. It was probably -- I don't remember.

Okay. So in summary, the rat studies show it takes, you know, in a rat about 20 times or more methylene chloride to get the same amount of carboxyhemoglobin as carbon monoxide.

We do know that carboxyhemoglobin is a serious problem for humans in terms of impacts on growth rate in

utero and, therefore, birth rate. The highest measured ambient was 4.8 ppb and we certainly consider methylene chloride to be an occupational hazard. I'm not sure I would have put accidental release.

The issues are it's definitely an occupational hazard and we have concerns about hotspots exposures, but we don't have data measuring concentrations near source. So it's something that we think the Air Board should look at.

PANEL MEMBER BLANC: So again here to summarize, the issue is completely based on exposure, because there's absolutely no question that methylene chloride is metabolized to CO and that there's a preferential childhood effect of CO. So here the entire argument rests on exposure potential, is that a safe summary.

SUPERVISING TOXICOLOGIST MARTY: I think that's a safe summary. In fact, if you look at the data it appears you need pretty high concentrations of methylene chloride to get significant carboxyhemoglobin. And there are reports of women who were pregnant poisoned by methylene chloride.

PANEL MEMBER BLANC: Well, and the other issue is that there's another nuance to that, which is that, as with arsenic where the issue is there are other sources of exposure, here we're talking about an additional source of carbon monoxide exposure and we know that people have an ambient source of exposure to carbon monoxide, independent

of methylene chloride --

PANEL MEMBER GLANTZ: You mean carbon monoxide --

PANEL MEMBER BLANC: Carbon monoxide, I'm sorry. So the issue is the contribution -- the potential additive contribution of methylene chloride to a child or neonate or fetal exposure that might be occurring through inhalation of carbon monoxide to begin with, with superimposed methylene chloride?

SUPERVISING TOXICOLOGIST MARTY: Yes.

PANEL MEMBER BLANC: I think that's important to put in context.

CHAIRPERSON FROINES: There's an important issue. I suspect you're familiar with the epidemiologic work that Beate Ritz has done in the last few years, specifically on reproductive outcomes of one low birth weight, low term and what have you relative to carbon monoxide levels?

SUPERVISING TOXICOLOGIST MARTY: Yes, we actually cited one of her papers.

CHAIRPERSON FROINES: Yeah, I saw that. And it seems to me that one should actually look at her work because it is so current and then ask the question, given what we know about methylene chloride, would it demonstrably increase the risk associated with the risk that she's demonstrated at extremely low levels of carbon monoxide? It's really a follow-up to what Paul is saying, because her

work clearly -- I won't say that, that gets you into trouble.

Her work suggests that -- and my feeling is that her work indicates an association with carbon monoxide, however, that association may be a surrogate for something else. As we know, that with air pollution lots of times what we measure turns out to be a surrogate for some other toxic exposure. But on the assumption that the carbon monoxide relationship that she's identified has meaning then it would make sense to look and see what the increased risk would be associated with an additional exposure associated with carbon monoxide.

PANEL MEMBER BLANC: So really we have two issues that are sort of emerging thematically. One is that there appears to be, and I think our findings will have to reflect this, there appears to be a series of priorities for the Air Resources Board to obtain data that relates particularly to hotspot emissions and correlating hotspot emissions that are reported in pounds with neighborhood air concentrations as opposed to ambient California air levels statewide.

And the second issue, in certain cases are situations in which perhaps sophisticated risk modeling in-house that your group could do, be it the contribution of a certain percentage of methylene chloride superimposed on ambient carbon monoxide or similarly a small amount of

ambient manganese or arsenic, and I guess we'll come up again with mercury.

Because the third arm of it is not something that's within your control, which is, you know, people need to go out and do, you know, differential epidemiologic or toxicologic studies in newborns or infants versus adult animals or humans. I mean that's not something that we can do anything about. But these other two areas are areas in which there can be some movement, I think.

SUPERVISING TOXICOLOGIST MARTY: Yes, we can do that. I'm not speaking for ARB.

That summarizes the six chemicals that came up at the last meeting. I should add that Dr. Froines asked us to make sure we'd gotten everything that was available on a few other chemicals and we did do that.

CHAIRPERSON FROINES: Dr. Froines actually emphasized very strongly the issue of naphthalene and so that was one that I feel pretty strongly about. But in a telephone conversation with Melanie she suggested that the methemoglobin issue was not a major issue, but that was a question.

SUPERVISING TOXICOLOGIST MARTY: It was a question. We did look at the literature on methemoglobin anemia in kids who had basically eaten mothballs and it looked like the concentrations of naphthalene these kids

were exposed to were in the gram per kilogram range. So pretty high concentrations.

We also actually -- Dr. Witschi brought up Charlie Plopper's work, the work that's going on in Plopper's lab, looking at naphthalene and Clara cell toxicity. And this is in post-natal and also adult mouse, showing that the Clara cell toxicity is elevated in the younger mice relative to the older mice.

So that's a very interesting area that's emerging. These concentrations are milligram per kilogram body weight range, so 20 all the way to 100, I think, were their doses. So these are, relatively speaking, high doses. And, Andy, was it -- it's inter-peritoneal?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Well, in general terms, I think this is IP.

CHAIRPERSON FROINES: You're going too fast. Go back to the -- can you help us understand this?

SUPERVISING TOXICOLOGIST MARTY: Okay, we're trying to get the staff person that just put these together. He stepped out for a second. But what Plopper's lab is doing is looking at naphthalene toxicity in the lung and looking at the difference between young animals and older animals. So, John, maybe you can explain --

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Dr. Budroe is going to take over at this point.

DR. BUDROE: Yes, basically you can see that there's a substantial difference in -- actually that should be ciliated respiratory epithelial toxicity in both seven and fourteen day old mice as compared to adults. And that's especially interesting because adult mice have roughly two and a half times the metabolic activation capability of seven and fourteen day old mice.

So the effective dose --

CHAIRPERSON FROINES: You mean p450 in those Clara cell?

DR. BUDROE: Correct. So the effective dose to the adult mice is actually greater than the effective dose to the neonatal mice. The toxicity you see in those ciliated epithelium cells is greater in the seven and fourteen-day-olds than in the adults.

The other interesting thing is, good point, that that's an IP dose. So what you're seeing isn't a contact effect, that's actually a systemic effect that's being expressed as lung toxicity.

CHAIRPERSON FROINES: Well, in that sense you know that work -- they're arguing that the p450 metabolism to the naphthaquinones is occurring in the liver and not in the lung, and so that this is a little more complicated than you're describing.

DR. BUDROE: Okay, the second slide is looking at

Clara cell toxicity in the different parts of the respiratory tract architecture. And you see a little bit of toxicity in the 14 day old mice compared to the lobar bronchi in the seven day old mice.

And what's actually happening is, you can see a change in compartmentalization. You're seeing enormous decrease in the nonciliated Clara cells and an increase in the compartment evacuated cells, which are essentially damaged cells.

So you're seeing this effect in a number of different respiratory epithelium cell types and in the number of different locations in the respiratory tract.

CHAIRPERSON FROINES: Following Paul's suggested approach, this meets both your criteria.

PANEL MEMBER BLANC: I guess you'd say that because this is one study there's not an extensive database for differential toxicity. Although I will say -- well, first let me ask a clarification. We've gone through a series of presentations previous to this, substances that your intent is to recommend for tier 2. We're going to come back later to how the documentation is going to be handled for the tier 2 substances so that it's consistent.

But leaving that aside, the naphthalene that you're just discussing now, could you clarify for me, is that something which you're also planning to propose as tier

2 or your argument here is why -- is this a clarification as why it's not coming to tier 2?

SUPERVISING TOXICOLOGIST MARTY: We've actually include naphthalene under PAHs, which is being recommended for tier 1.

PANEL MEMBER BLANC: Okay, so this will fall into the tier 1 argument.

The other issue I would say, and why it may be helpful to have this two column evaluation, the issue as to what the dose is that induces methemoglobin in the case reports of an ingestion of naphthalene is not the issue. That's an issue in terms of whether exposure levels would ever get up to that area.

SUPERVISING TOXICOLOGIST MARTY: Correct.

PANEL MEMBER BLANC: So your issue in pediatric sensitivity is, in fact, if you gave an adult versus a child the same amount in milligrams per kilogram, whatever that dose is, would children develop more methemoglobin anemia and that's the data you have to look at, based on the function of methemoglobin reductase. I'm assuming that infants would be more sensitive.

So from a pure biological point of view you have, I believe, put emphasis really parallel to the carbon monoxide issue in fetal hemoglobin binding of carbon monoxide. It's really not a biological issue. Then you're

completely pushed in to the exposure issue and is there significant exposure at levels where this would be a health effect that would matter.

SUPERVISING TOXICOLOGIST MARTY: Yes, that's --

PANEL MEMBER BLANC: I just want to clarify that, unless I've misunderstood.

CHAIRPERSON FROINES: Roger Atkinson measured levels of naphthalene in Glendora at 3600 nanograms per cubic meter, which isn't by any means trivial, and so how does that exposure finding relate to what Paul is asking?

SUPERVISING TOXICOLOGIST MARTY: I'm not sure I can relate it directly to the methemoglobin anemia issue other than to say that from the case reports these kids had really high exposures. We don't have information on what would happen if adults had gotten the same type of exposure. You know, at the microgram per cubic meter amount, you'd have to inhale an awful lot to get up to the gram per kilogram range.

We did -- if you'll recall our chronic REL, our chronic REL is about at the levels that Dr. Atkinson is measuring, so we did have some alarm bells go off then. And that's actually based on, if I'm recollecting correctly, respiratory epithelial damage end point.

CHAIRPERSON FROINES: I don't remember and I suspect nobody else does, but did you use Charlie Plopper's

work in your REL determination?

SUPERVISING TOXICOLOGIST MARTY: No.

CHAIRPERSON FROINES: So that you probably have to go back and relook at that number.

SUPERVISING TOXICOLOGIST MARTY: Yes.

CHAIRPERSON FROINES: Because it may be -- your number may be too high relative to the current information available to us.

SUPERVISING TOXICOLOGIST MARTY: Yes, we need to go back and look at that.

PANEL MEMBER WITSCHI: I have a couple of comments. First of all, that's not all there is to the naphthalene story. There actually are data out there in which they did inhalation. So if you're worried about high milligrams per kilo, I don't know the numbers offhand, but you might want to look up the inhalation study stated.

The other thing is there's really much much more to the naphthalene story than just this one single paper.

SUPERVISING TOXICOLOGIST MARTY: We realize that.

PANEL MEMBER WITSCHI: Because if you look up the whole body of work that has been done over the last ten years then you have a tremendous lot of information in difference species at different ages.

SUPERVISING TOXICOLOGIST MARTY: Yes, we're aware of that.

CHAIRPERSON FROINES: This issue is very troubling. I agree one hundred percent with Peter. And, you know, it is one of the central elements of our research in Southern California, because we identified fairly significant quantities of naphthaquinones in the air in Southern California. And that has a great deal of significance with respect to the production of reactive oxygen species. And so that we think naphthalene is an extremely important compound from the standpoint of respiratory effects in children.

You know, sometimes it's good to be a lumper and sometimes it's good to be a splitter. And in this case to lump naphthalene at 3600 nanograms per cubic meter with Benzo[a]pyrene at half a nanogram per cubic meter is really a complete misunderstanding of a different significance.

I mean Benzo[a]pyrene is an important carcinogen, yes, that's fine, but the reactive oxygen chemistry associated with naphthalene is so important that, for us to just kind of lump it with all the other PAHs, including things like pyrene which obviously have very low toxicity is really problematic I think.

I don't think we can just put naphthalene in there with PAHs and kind of then forget it. It's just too important at this point. And our work is showing it and Charlie Plopper's work is showing it, you know, and so I

think we need an alternative approach to this one.

DR. ALEXEEFF: George Alexeeff. We haven't quite gotten to the point of maybe discussing, you know, how chemicals should be expressed on Tier 1 and Tier 2. But I think our point was we felt there was enough evidence for this and other PAHs to be in Tier 1. Okay, that was our bottom line point.

Specifically what we were thinking, again we haven't gotten to this part, but just to address your point, under polycyclic aromatic hydrocarbons we felt we should specifically list those for which there were data and this is one of those that are listed. And then that might address your concern.

So it's not hidden, it's specifically listed as a chemical.

CHAIRPERSON FROINES: So that within the document on PAHs that we may have some sections that address specific toxicities associated with particular chemicals?

DR. ALEXEEFF: Yes.

PANEL MEMBER BLANC: That being said, that's reassuring, that we're going to come back to the draft potential structure of our findings, but since that draft, I assume, represented a collaboration trying to emphasize the key points, you know, naphthalene under five, naphthalene doesn't receive any mention whatsoever separately, nor are

the airway effects of it mentioned. So the findings vis-a-vis polycyclic aromatic hydrocarbons are driven largely by the carcinogenicity issue and then --

SUPERVISING TOXICOLOGIST MARTY: That's why it's a draft.

PANEL MEMBER BLANC: I know, I'm just saying, let's bear this in mind, because --

SUPERVISING TOXICOLOGIST MARTY: Yes.

PANEL MEMBER BLANC: -- I support the statement you made, but let's make sure that we're consistent.

PANEL MEMBER WITSCHI: And I think it's getting messy. You know, we are dealing with categories on one side, and we are dealing with something else on the other side. Why don't we just deal with PAHs, with metals, with organic chlorine compounds, with all those kind of things. It's really getting messy.

CHAIRPERSON FROINES: Believe me, if we could do that we would have done it two meetings ago, because some of us are big believers in aldehydes.

(Laughter.)

CHAIRPERSON FROINES: And we would have had an aldehyde category, but I've asked that question of George and Melanie 25 times and been told and spanked each time, saying, no, we can't deal with classes of compounds, with the exception of PAHs, because --

PANEL MEMBER WITSCHI: What's the reason for that one?

CHAIRPERSON FROINES: -- because of the fact that we can only list compounds that are listed as TACs and PAHs are listed as TACs and aldehydes as a class are not.

PANEL MEMBER WITSCHI: I'm sorry, this might be before my time, when did they list PAHs as TACs? I do not recall having done PAHs.

CHAIRPERSON FROINES: That's a good point.

DR. ALEXEEFF: We presented a document to the panel in '93 on Benzo[a]pyrene and a number of polycyclic aromatic hydrocarbons. At that same time another law required us to adopt all of the hazardous air pollutants that UCPA listed as TACs and that's how really all the other PAHs came in. And then so in the actual listing that the Air Resources Board did they listed it under the great group of POM, polycyclic organic matter.

CHAIRPERSON FROINES: We had POM under the HAPs, the Clean Air Act amendments in 1990 and then we had BAP, but we listed maybe 20 other compounds in terms of their relative potency, so in a sense we -- you're right though, you're absolutely right. It was BAP that we formally listed.

Let's take a ten-minute break.

PANEL MEMBER GLANTZ: Before we do that, are we

going to go on and start talking about the findings next?

CHAIRPERSON FROINES: No, we're going to go on and talk about the documents -- I believe we're going to talk about the revised documents that they've submitted to us.

PANEL MEMBER GLANTZ: Okay, can I just say one word about the findings, what we handed out, just so people are looking at it. Just so the people on the Panel know kind of what we had in mind when I worked with OEHHA on the findings.

It was clear that the final list of five hadn't yet been determined. So the way the findings are structured is finding number one, which you notice has a big blank, is what are the five. And then the next ones are little summaries, which can be edited and amended by the Panel, of the seven compounds that it seemed to us were likely to be the ones from which the top five emerged.

So what we would do in addition to any editing of those is two of those will be removed from the top five. Then what is now finding number eight is a place to say basically that there's several other toxic air contaminants that are of particular concern, which are what we've been calling Tier 2 and then we've done little similar summaries for those. And if someone wanted to move one of those up to Tier 1 I guess we could.

And then I also included, in light of the

extensive discussion at the Panel, just a comment about environmental tobacco smoke.

The one thing that isn't in here that we had discussed that we'd all forgotten about was a comment about pesticides and if we want to add that somebody will have to draft something up. So just when you're looking at it, just -- because this is a little different than the way they usually come back.

CHAIRPERSON FROINES: So the plan right now -- let me just, before we take a break, the plan right now, Melanie, is one, you're going to go over the chemicals that you have supplied, revised documents. Then we're going to have a comment or two, I think from Colleen on some legal issues with respect to the determination of how we proceed, given that these documents have not been sent out for public comment and issues of deciding what are five or what are ten or whatever. And then we'll go and discuss the findings.

And the other thing that I want to mention here is that since there are only five Members of the Panel, the administrative matters on the agenda I think we'll defer to a future meeting when the number of panelists are -- when we have a more full panel. I'd rather discuss administrative issues when we have everybody here.

So that's the plan for the day unless you have a major disagreement or the Panel does.

PANEL MEMBER BLANC: The only thing I'd add to that is that in the context of that first discussion to get a sense from you of your plan for dealing with the written documentation for the other Tier 2 chemicals for which there is not yet written documentation. So that I'm quite concerned that we have a consistent and symmetric approach in terms of the written documentation.

SUPERVISING TOXICOLOGIST MARTY: Okay.

CHAIRPERSON FROINES: Let's just break for about ten minutes.

(Thereupon a recess was taken.)

DR. ALEXEEFF: What we thought we would do next is, there are some -- after presentations and some discussion and some feedback from the Panel there are some chemicals that were on our group of 11 that we feel really are not likely to make this list of five, so we thought we would just try to take those off the table now just to let you know which ones we don't think are necessarily in play anymore, just to help focus our discussion.

They would remain in Tier 2 and we'll explain briefly why.

CHAIRPERSON FROINES: And we'll come back later to the issue of comment period and review and all of that.

DR. ALEXEEFF: Right, we'll come back later for that.

And then we also need to make a presentation in dioxin, which will be a little bit lengthy because the Panel hasn't heard the dioxin information.

CHAIRPERSON FROINES: And following Paul's -- what's that word, paradigm, it can be hopefully focused so it doesn't have to be too long.

DR. ALEXEEFF: Well, there just is a lot of data.

CHAIRPERSON FROINES: The Panel will clearly be interested in the second half of the paradigm on exposure.

SUPERVISING TOXICOLOGIST MARTY: For the proposed Tier 2 TACs that we think just won't make the top five, I'd just like to just briefly go over which chemicals those are and why we don't think they'll make the top five, and I don't have overheads for this.

But vinyl chloride we think has sufficient data based on the studies done looking at increased potency in neonatal animals. But there's not enough exposure to shout about, so it's one of those where, if there were, for example, if there was a great big facility that was emitting lots of vinyl chloride then we would definitely be concerned, so we encourage continued tracking of vinyl chloride emissions in the state, but at this point we think it should stay in Tier 2.

Noncoplanar PCBs are another group that we think has actually fairly strong evidence for differential

effects, but there are virtually -- well, I wouldn't say no, but there are extremely limited airborne emissions and most of the PCBs are out there in the environment in reservoirs, and I don't mean water reservoirs, just from past production and past distribution throughout the environment, and there really isn't very much being emitted anymore directly.

Glycol ethers, we think have fairly strong evidence, based on teratogenicity in animal models, but it's unclear how much exposure there actually is. There are significant hotspots emissions. These compounds are not monitored routinely in the air, so we have very limited information, in fact none, on what would be an ambient concentration on any of the glycol ethers.

CHAIRPERSON FROINES: Melanie, on that issue, I sent you a note a long time ago which was, you probably didn't worry too much about, because of other priorities, but I actually think it would be useful to go to the semiconductor association and actually ask them how much of those glycol ethers are still being used. Because clearly in the seventies and early eighties the semiconductor industry got rid of those compounds and it would be interesting to find out to what degree do they think there is still some use, because I think that would probably be the area that would drive it. And I don't know how much there is still used in printing and inks and other kind of

solvent mixtures and that's obviously information that's harder to get a handle on.

The other comment I was just going to make on glycol ethers is again in the occupational health world there are numerous case studies of neurobehavioral effects in 1973 when acetone was replaced with glycol ethers because of the energy crisis, which is an interesting question given our current energy crisis.

So that the neurobehavioral effects seem to me to be still a very very important end point for glycol ethers.

SUPERVISING TOXICOLOGIST MARTY: Finally in Tier 2 we had mercury, which is a developmental neurotoxin in humans. The evidence is extremely strong. I don't think there's any debate about that.

The issue in California is fairly low airborne exposures. There are significant exposures via food, primarily fish, so that too, I think it's an important issue in California, but it's more from a waterborne perspective, much more, than an airborne perspective.

We do have some emissions in mercury from incineration sources, including municipal waste incinerators, which seem to be the largest sources of mercury emissions, at least in the Air Board's database, and also some emissions from hospital waste incineration.

Mercury still is definitely a cause for concern.

If there were more emissions it would be a slam dunk to be in Tier 1.

PANEL MEMBER BLANC: Can you quantify then -- I know you had a slide that you had prepared for the last presentation. Can you quantify the amount of mercury in those hotspot emissions?

SUPERVISING TOXICOLOGIST MARTY: Yeah, the total is about 10,000 pounds statewide. Some of the bigger sources, I know we have a slide -- okay.

Okay, we have a large resource recovery facility in Long Beach. It's 688 pounds per year emitted and also the commerce, municipal waste incinerator is about 108 pounds per year. And then we have a fairly large medical waste incinerator in Sacramento with about 45 pounds per year.

PANEL MEMBER BLANC: And are those the only incinerators in the state of California?

SUPERVISING TOXICOLOGIST MARTY: No, there's probably six or seven municipal waste incinerators and there's a few, in fact, there's a medical waste incinerator in Oakland, and I'm sure there's a few other medical waste incinerators.

When the dioxin airborne toxic control measure was developed, because medical waste was the source of dioxins, it sort of changed the paradigm of how medical waste was

incinerated and went from numerous incinerators that were poorly run, usually on site, to very large state of the art facilities. So the total number is much smaller than it used to be.

PANEL MEMBER BLANC: So the data that you have here don't imply that there is no emissions from the others, it's just that the others haven't been measured?

SUPERVISING TOXICOLOGIST MARTY: The others have lower emissions. What we did was pick out a few of the highest emitters.

CHAIRPERSON FROINES: And then the total -- and so what's the total pounds per year in all of them?

SUPERVISING TOXICOLOGIST MARTY: The total from the air toxics emissions database for 1998 was 10,000 pounds, all sources, not just incinerators.

PANEL MEMBER BLANC: And what's the total amount of that from incinerators?

SUPERVISING TOXICOLOGIST MARTY: We have to add it up. We have a list of a large number of incinerators, and these include crematoria, because you're -- so I could have somebody add that up and then we could give you the answer.

PANEL MEMBER BLANC: Well, I guess the reason why I'm asking you the question is I want to get a sense similar to the question with arsenic. Although it's slightly more complex because -- in fact the original source of most of

the mercury that gets into the food chain through the fish or a source of a lot of it could have been airborne deposition, so it's airborne exposure that then eventually gets to us through dietary exposure, although it's historical, I suppose.

SUPERVISING TOXICOLOGIST MARTY: Yes. In California actually probably the largest contribution has been gold mining, because, we, you know, a hundred years ago took the mercury out and used it in the gold mines, so it's gotten virtually everywhere in the valley and even in estuaries. And so with uptake by fish that's then the source of human exposure.

PANEL MEMBER BLANC: So what percentage, you know, we had talked earlier about the percentage of an airborne source to the total that would be of concern. Have you got some sense of what 10,000 pounds of mercury is proportionally in terms of the exposure per capita to mercury per year?

SUPERVISING TOXICOLOGIST MARTY: Well, we have actually, the concentrations measured in ambient air are around one to four nanograms per cubic meter, on that right-hand column and those represent maximums for specific monitoring network sites.

What did I just say? Did I not say mercury? Whatever I said I meant mercury.

So it's about 30, say 30 nanograms per day at the peak concentrations that have been measured.

We did an analysis under Proposition 65 looking at consumption in kids of mercury from tuna and George is trying to remember the number. It's quite a bit larger than 20 nanograms per day or 30 or even 40.

PANEL MEMBER BLANC: It would have to be -- I mean if it was only ten times larger, if it was 200 nanograms per day, for example, that would mean that you were getting ten percent, so then that would be something worse. It was a thousand times larger then it would mean that it's .1 percent and then we would sort of fall below our -- I mean isn't this something that needs to be written out and spelled out explicitly in your written documentation?

SUPERVISING TOXICOLOGIST MARTY: Yes, we will do that.

PANEL MEMBER BLANC: But it is your impression that we're talking about some trivial percentage?

SUPERVISING TOXICOLOGIST MARTY: Yes.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: A lot of the dietary mercury from within California it appears to -- I can't give you an exact number on this, but it appears to ask to be coming by emissions which are directly into water rather than directly into air in the first place. And I believe I'm correct in saying, for

instance, that a major source of the contamination of Clear Lake, for instance, which is known to have a mercury problem, is a result of mine outflow.

So that, we need a quantitative figure on that. But I think I'm correct in saying that that's the major source, not emissions to air in the first place.

PANEL MEMBER BLANC: I mean I was asking an even more simplistic question. I was just assuming that none of the air then got into the fish, I was just assuming that whatever --

SUPERVISING TOXICOLOGIST MARTY: Oh, no, there's a certain cycling of mercury that happens that way. Yes, you definitely get deposition.

PANEL MEMBER BLANC: I know, but I mean even if you take that out of the equation, just in terms of people's exposure via inhalation as opposed to their dietary exposure, is it less than one percent?

SUPERVISING TOXICOLOGIST MARTY: I am remembering it's less than one percent, but we can actually figure that out at lunchtime and get back to you on that.

PANEL MEMBER GLANTZ: While you're eating your tuna sandwich.

(Laughter.)

CHAIRPERSON FROINES: This is always the danger, of course, in allowing yourself to get caught taking up

rules of thumb, because then they come back on you at some point and you have to live with them.

But did you do a ratio of your REL for mercury with your airborne concentrations?

SUPERVISING TOXICOLOGIST MARTY: Yes.

DR. ALEXEEFF: Looking at the doses that we normally see, we'll double check this, but it looks like it's about a 100 to 300 fold ratio between the oral consumption, primarily through seafood versus inhalation. But we can double check that here today -- well, certainly in the document, we can put that in there.

PANEL MEMBER FUCALORO: There is no ratio of ambient concentration to REL for mercury in your tape?

DR. ALEXEEFF: No.

SUPERVISING TOXICOLOGIST MARTY: I just discovered that.

(Thereupon a short discussion was held off the record.)

SUPERVISING TOXICOLOGIST MARTY: Okay, we're going to get you that ratio also.

CHAIRPERSON FROINES: What was the airborne concentration, George, do you remember?

DR. ALEXEEFF: About 20 nanograms per day.

SUPERVISING TOXICOLOGIST MARTY: Twenty to Thirty. It's about one and a half to two, right in there, have been

the ambient average concentrations of the data that we could get hold of. So if you assume X numbers of cubic meters per day, you can get 20 to 30 nanograms.

PANEL MEMBER FUCALORO: You're not giving a concentration, you're giving an uptake, is that right?

SUPERVISING TOXICOLOGIST MARTY: Right.

PANEL MEMBER FUCALORO: Okay.

SUPERVISING TOXICOLOGIST MARTY: That assumes, of course, one hundred percent absorption, etcetera.

CHAIRPERSON FROINES: What's the airborne concentration in the Los Angeles basin, for example?

SUPERVISING TOXICOLOGIST MARTY: 1.5 at North Long Beach's monitoring station. Well, it's four at Riverside.

PANEL MEMBER FUCALORO: 4.0 nanograms per meter cubed. And then what factor are you multiplying that or dividing that by in order to get the nanograms per day?

SUPERVISING TOXICOLOGIST MARTY: Twenty cubic meters per day, and that would be an adult exposure, per 70 kilograms.

PANEL MEMBER FUCALORO: And what does it come to?

SUPERVISING TOXICOLOGIST MARTY: So that would be, if there was four nanograms per cubic meter and you were inhaling 20 cubic meters and you assume 100 absorption then you're getting 80 nanograms, at the peak site. And those actually aren't the averages, those are the maximums

measured in a year, in one of the years, '98 it looks like, at that particular monitoring site.

CHAIRPERSON FROINES: I don't want to get into something that's more complicated, but what's the form of the mercury that you generally think is released from these sites? Is it mercury metal or is it mercury salt?

SUPERVISING TOXICOLOGIST MARTY: It's both. You can get elemental mercury coming out of the incinerator's vapor, as a vapor. You can also get chloride salts and other salts.

CHAIRPERSON FROINES: And do you have any idea what the particle size of the mercury is, of those materials?

SUPERVISING TOXICOLOGIST MARTY: Well, for the elemental, of course, it's just coming out, it escapes the bag house completely. There is some collection of the smaller particles in the bag houses, but not being an engineer I don't know the efficiency with respect to the size of the particle, nor do I know the size of the particles that are coming out.

CHAIRPERSON FROINES: I'm just trying to think about what the relative amount that's absorbed through the gut or not absorbed through the gut, as the case may be versus respiratory uptake.

I'm at a level of too much detail, so why don't we

go on.

Unfortunately this is an important issue, as we all agree, because the evidence is so strong on the health side.

SUPERVISING TOXICOLOGIST MARTY: Exactly.

Okay, in terms of the chemicals that were in the original 11 that we wanted to move, we need to mention that benzene was -- we got a lot of public comment on benzene and we agreed in large respect with a lot of the comments and think that the epidemiology evidence, which we were trying to hang our hat on, is relatively weak, and that is the evidence of parental exposure being associated with elevated incidents of childhood leukemia.

So we have decided at this point, amongst ourselves, that we would not recommend benzene for Tier 1.

CHAIRPERSON FROINES: Just one question and then we can go on. You're comfortable with the differences in childhood leukemia versus adult leukemia and benzene associated leukemia, because that's obviously a key question. Do you know what I'm say?

SUPERVISING TOXICOLOGIST MARTY: Yeah, I'm probably not the right person to answer the question, but I know -- yeah, we're not exactly, we're not willing to say benzene doesn't induce leukemia in children, because the type of leukemia kids get is different than the type of

leukemia seen largely in the benzene exposed workers. We're not saying that. I don't think that that's something that you would -- I don't think there's a lot of evidence that therefore it doesn't influence rates of childhood leukemia.

PANEL MEMBER GLANTZ: This was the one where I was quite impressed with the public comments and the arguments that the evidence was not as strong as for other things. I mean I don't think anybody is suggesting it be taken off the list, you know, that it be dropped out of Tier 2. But I think given that we can only pick five, I just think the evidence on benzene is -- there are five other things where the evidence is much stronger that it's important than for benzene.

So I agree with OEHHA's recommendation. In fact I think I suggested it at the last meeting or two ago.

SUPERVISING TOXICOLOGIST MARTY: We do have a ratio of the ambient concentration. This is a statewide ambient of 1.9 nanograms per cubic meter ratioed to our chronic REL which is .09 micrograms per cubic meter and that ratio is about .02. That's ambient, though, it's not near source and the near source is what we were worried about.

The next thing we would like to do is the Panel has not heard our presentation on dioxins yet, so --

PANEL MEMBER FUCALORO: Excuse me, were you going to go through some of the -- I thought, and maybe you just

did, go through some of the chemicals that would not make Tier 1, because I have here something that was handed to me on acrolein. I was wondering if that was part of your presentation?

SUPERVISING TOXICOLOGIST MARTY: That's going to be part of the presentation coming up.

PANEL MEMBER FUCALORO: Oh, coming up. Okay. I'm just kind of losing sight of where we're going at the moment.

SUPERVISING TOXICOLOGIST MARTY: Peter, does the Panel have the dioxin's handout? Okay, because that's what we're going to do next.

(Thereupon a short discussion was held off the record.)

SUPERVISING TOXICOLOGIST MARTY: Okay, so following the dioxin presentation we're going to go and give a very brief overview of the presentations you've already heard on five other substances that we think are important, as well as a comparison between acrolein and formaldehyde, which was asked for earlier, if the Panel wants to hear it.

CHAIRPERSON FROINES: This has been in contrast to earlier meetings, very relaxed and very well articulated and I think in general, everybody is happy with the way the meeting is going.

I think that the one thing I need to say at this

point is that it's five to twelve. We're going to have to really move along because we don't have that much time and we need time for deliberation. And so I really think that you're going to have to hold down the length of the presentation as much as possible, albeit trying to meet Paul's criteria, you know, at the same time. And I'm one of the worst persons on this of getting off on sidetracks and so the Panel will also try and avoid going off.

Melanie, before you start on dioxin, could you explain to the Panel why, if you have dioxins and coplanar PCBs as part of your list, why you could not also include noncoplanar PCBs?

SUPERVISING TOXICOLOGIST MARTY: We actually could just list dioxins and PCBs. I think the issue is, for us, that the environmental burden of dioxin-like PCBs is significant enough to increase the overall impact of dioxin and dioxin-like compounds. And what we're trying to do is distinguish from the toxicology information that noncoplanar PCBs do not act like dioxin. They have their own developmental neurotoxicity.

PANEL MEMBER FUCALORO: Except if they're polychlorinated, is that the issue?

SUPERVISING TOXICOLOGIST MARTY: It's the planarity of the ring and it depends on where the chlorines are in each --

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I'll be explaining this, I hope.

PANEL MEMBER FUCALORO: Because noncoplanar PCBs are included here, right?

SUPERVISING TOXICOLOGIST MARTY: They're included in the summary, yes, you're correct about that.

PANEL MEMBER FUCALORO: And I think the reference is dioxin-like.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: No, there's two classes of PCBs, which I will attempt to clarify.

PANEL MEMBER FUCALORO: Fair enough.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Well, I'll try and run through this as fast as I can consistent with clarity.

The presentation I'm giving you is about specifically the dioxin-like compounds and we propose that these be placed in Tier 1, because we had high concerns over the toxicity about point source emissions and background levels of some of these compounds and the potential for bioaccumulation.

We found evidence of differential impacts on children in relation to immunotoxicity, developmental toxicity, endocrine effects and we also, since infants are highly exposed via breast milk, we also have concern for the

established carcinogenicity of these compounds.

Although current air levels are low, air is the primary transport medium for new emissions of dioxin-like compounds. These compounds show extreme bioaccumulation and environmental persistence and the current multi-pathway exposures in California are high and may, in fact, exceed the effects levels.

I'll explain briefly what I'm referring to here. The dioxin-like chlorinated compound --

PANEL MEMBER WITSCHI: Just a question, how come again we have a class of compounds?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Because this -- we have listings of classes in the toxic air contaminant program. We have actual listings of dioxins and PCBs as named classes in the regulation. This is also, as we were saying earlier, like the case of the POM, which is the defining class for the polycyclic aromatic hydrocarbons. Fortunately or unfortunately it's not, for instance, listed in that way for reactive aldehydes or something like that. That's the critical distinction.

However, we do actually have a problem with the way the TAC listing is done for the dioxins, which is where the PCBs basically cover two groups of chemicals which are separate in their biological effect. And I'm referring specifically here to the coplanar PCBs and not the

noncoplanars.

This is an example of a noncoplanar where the presence of an ortho substituent results in the molecule having a twisted confirmation in its ground state and this results in different biological activity. So, for this purpose I'm not referring to these compounds.

Sources of the dioxin-like compounds, especially dioxins, include combustion, from various forms of waste incineration, and there's currently considerable interest in that backyard burn barrel situation. It's being looked at by the US EPA and the Air Board.

There are some minor sources, such as metal smelting and refining. Formerly bleaching of wood pulp was an important source involving release to water, but this is now much reduced due to the replacement of chlorine by other bleaching agents.

There is also concern about contamination of waste sites, old manufacturing sites. And in the case of contaminated areas you may actually get resuspension of dioxin containing particulates back into the air.

As far as the contamination of the environment is concerned, obviously sediments form an important reservoir of dioxins, and because of the bioaccumulation, the biota are significantly contaminated, including both sport and commercial fish and game and also meat and dairy foods and

human milk.

Most -- the figure of greater than 90 percent was recently derived based on measurements by US EPA. More than 90 percent of the newly formed dioxins are released directly into the air and then proceed to bioaccumulate in the food chain. Food is the major source for both the PCB and dioxin elements of this group.

And exposure begins at an early age with breast feeding, where this study, Patandin, et al, '99 study was a study of breast fed infants exposed to background environmental levels of dioxins. And it's been calculated that an average breast fed baby receives a considerable excess of the dioxin-like compounds relative to what we consider our current standard.

These amounts are expressed as what we're calling TEQ. This is the dioxin equivalents using the toxicity equivalency factors from the table. So the breast-fed baby is receiving 40 pg per kilogram of dioxin equivalent per day relative to the chronic or REL of 10 pg per day.

SUPERVISING TOXICOLOGIST MARTY: That's based on measurements of dioxin equivalents in the breast milk.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Also, as young children consume a greater proportion of their diet in the form of dairy foods and manufactured foods, which are important sources of dioxins,

they tend, actually, to receive rather higher exposures than adults.

There were three times higher exposure of toddlers than adults in the Patandin study. And the breast-fed infants were receiving 50 times higher than the adults.

The effects of dioxin-like compounds, I'm going to start by reviewing the effects, which have been shown in humans. First, the immunotoxicology, the typical findings are changes in the number and activity pattern of the T cells and these changes at the cellular level are reflected in functional changes in the antibody response. And both the response to common diseases and also incidents of things like ear infections, and also, interestingly enough, a lower prevalence of allergic disease.

So this actually represents quite an interesting disturbance of the normal development of the immune system. This has been seen both in the -- for instance, the Weisglas-Kuperus study. This addressed children exposed to background levels.

And also, of course, in a more extreme form these same effects are seen in infants exposed to high levels as a result of specific contamination incidents, such as the Yu-Cheng incident which is reported by Chao, et al.

PANEL MEMBER WITSCHI: I have a question, in any of those upcoming human studies and the present ones, are

there any data which came out of the incidents in Seveso?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Yes.

PANEL MEMBER WITSCHI: And could point those out to me?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I will do so.

There are suggestions of an adverse developmental impact. These have been described by Patandin and coauthors in terms of vastly reduced birth weight and secondly reduced growth during the first three months of life. And there's other reports also of similar effects.

This is the Seveso aftermath data that I wanted to draw your attention to. Obviously there are a number of reports now coming out on the survivors of the Seveso incident. This one is of particular interest. It appears that there's an alteration in the sex ratio of the offspring of fathers exposed during childhood to the TCDD which was emitted in Seveso.

So this is a developmental effect as a result of childhood and it's impacting a parameter which is generally considered to be an extraordinarily robust feature of normal human reproduction. There's something going on here. We don't understand the mechanism. It presumably is somehow linked to pertobation of the endocrine system during the

development and maturation of the reproductive system.

But, beyond that, I don't wish to speculate as to what the mechanism might be, but clearly this is a highly-significant effect and it is a specific impact on children. The fathers exposed in adulthood showed a much less significant effect.

I'm going to attempt to briefly review the effects of dioxin-like compounds on animals. There's clearly a very large literature and I'm specifically picking only a few recent reports and those reports which parallel the effects I've pointed to in humans.

Firstly, immunotoxicological. Again, the changes in the distribution of the T cells and changes in the functional behavior of the immune system. These are in rats exposed to TCDD in utero and via lactation. These effects were persistent into adulthood well after the time at which the dioxin to which the rats were exposed would have been cleared by a metabolism and excretion. So this is a persistent developmental effect.

Other reports showed similar findings, changes in splenocyte, suppression of delayed type hypersensitivity. And again these are, to a varying degree, persistent past the immediate post-natal period into adolescence and adulthood.

The developmental effects observed in rats include

a number of specific teratological changes in addition to the more general growth retardation type of effects which have been reported in humans. Interestingly, several of the specific effects observed here actually do have implications for the developing reproductive system.

Another teratological effect was the observation of ototoxicity in rats exposed to a PCB mixture, A1254, which includes a substantial dose of coplanar PCBs via the lactational route.

This is a further report on the effects of dioxin-like PCBs. Again we're seeing changes in both morphology and function of the reproductive system. Also changes in brain weight and reduction in serum testosterone. These animals were exposed to specific coplanar PCBs in utero and via lactation. And then these effects were assessed at post-natal day 65 or 140, so they're consistent into adulthood.

CHAIRPERSON FROINES: Can I just ask a quick question. Based on the Seveso data and the sex ratios, has anybody tried to do some animal experiments to look at that issue?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I'm not personally aware of such an experiment.

PANEL MEMBER WITSCHI: I would like to come back to the Seveso incident, you know. I mean we have here one

set of data, a late effect. But at the time being this created some excitement and are there no information whatsoever available on what happened to this population within the ten years, the first ten years after exposure?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: There's been a considerable amount of epidemiological studies and --

PANEL MEMBER WITSCHI: What did they say with regard to children?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: There are no other clear and unequivocal findings that we could identify. There's a lot of interest about issues like cancer and --

PANEL MEMBER WITSCHI: So if this acute high exposure had done something substantially to children we should know, but it didn't.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Well, there are, unfortunately, some fairly major problems with the epidemiology of the follow-up to the Seveso incident. We're only now beginning to see things coming out with a reasonable degree of certainty.

There were certainly some very significant causes for concern when looking at incidences of cancer, including leukemias and various measures of birth outcomes and so on. But, unfortunately, I think at least partly due to the

epidemiological difficulties, we don't have clear statistically unambiguous conclusions on all of those things at this point.

So I think the general feeling is that there are things going on in that population, but it has proved very difficult to establish exactly what they are.

PANEL MEMBER WITSCHI: Well, this could mean two things.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: There's a considerable folklore as to what the nature of those difficulties are.

PANEL MEMBER BLANC: Well, let's put this in context. In terms of our handout here of various slides on this, we're actually quite -- you have three more slides after this. So let's do those and then let's try to put it into context.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Right.

Okay, well, the report here is an interesting finding. This is actually a finding of transplacental cancer promotion. Rats were exposed to TCDD in utero. In the 50-day offspring the first observation was morphological. These were female rats and there were morphological changes in the mammary gland.

But in addition to that the mammary gland was more

susceptible to the induction of mammary adenocarcinomas by a single dose of DMBA. This graph actually shows the tumor incidents, cumulative incidents after the single dose of one microgram of DMBA.

This is a fairly small dose, and it's clear that the TCDD rats, which were treated in utero are at 50 days postpartum, still substantially more susceptible to the tetranogenic effect. And at this point, 50 days postpartum, we're not talking about residual TCDD here. We're talking about some persistent biological change in, as noted previously, the morphology, and evidently also the growth regulation of the mammary gland.

I wanted to just briefly refer also to another hormonal effect which is the thyroid hormones. The noncoplanar PCBs are characterized by different impacts on the thyroid hormones. But I'm going to concentrate on the coplanar effect here.

There is, in fact, a reduction in T3 and T4 levels, both in the -- well, this report is specifically in humans, but this is a response to the PCD, the dioxins, the dibenzofurans and the coplanar PCBs. It's not, I think, 100 percent clear what the mechanism is, but it may involve actually enhancement of T3 metabolism, and that effect has also, I think, been reported in animal studies.

But, anyway, I'd like to summarize what we know

about the mode of action. The important message here is that there is a so-called dioxin-like mechanism at work with all these compounds which involves interaction with the so-called Ah receptor. This triggers a suite of biochemical responses which includes cyt P450 induction. The iso enzymes varying with tissue and species.

That receptor interaction is also accompanied by characteristic toxic responses, specifically immunotoxicity, teratogenesis and carcinogenesis. And these correlate with the interaction with that receptor.

Some of the other toxic effects do not correlate strictly with the Ah interaction, so there's a possibility that there's another receptor which responds to dioxin-like compounds or possibly an indirect mechanism, which may involve endocrine effects.

But we consider that all these aspects of the mode of action have important implications for the both pre and post-natal development of infants and children.

And that's the end of my presentation.

PANEL MEMBER BLANC: Well, two things strike me about this presentation. One is that considering that dioxin is one of the most elaborately studied toxins in literature, the direct evidence of preferential childhood effects as opposed to the fact that children as well as adults have effects of dioxin is not overwhelming. There's

just a lot of interesting stuff which would have implications for children, more or less, if you had to characterize the bulk of the literature, and that's particularly so for the epidemiological literature.

But the second thing that was even more striking from your presentation is I don't see anything here on the second axis, which is current airborne release. I understand the point that historically most of the dioxin and dioxin-like substances which are in our food chain originally got there through various airborne sources, although some of them probably did get there through waterborne sources, particularly from the bleaching in the pulp industry, where that was a waterborne release, by and large, not an airborne release.

But where -- in the written document I see that there are approximately 60 pounds a year that were released in 1996, something under 60 pounds in California. I mean these statements are not adequate it seems to me to address -- a lot of these are historical issues. Where is the evidence to say that there is currently --

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: There are current and ongoing releases of dioxins.

PANEL MEMBER BLANC: You're showing less than 60 pounds a year. Compared to the amount that's in the environment currently, that's certainly not a biologically

significant contribution, is it?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I think actually -- well, given how long these materials persist, and I think it seems that the level of dioxin release into the environment has been reduced somewhat, but when we're talking about the current level of airborne releases, I think that is generally still considered to be of concern in relation to not adding to the already excessive burden.

PANEL MEMBER BLANC: Why doesn't that argument apply to mercury then where you have, what is it, a thousand pounds of mercury going up into the air?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: It's difficult to compare -- I mean a thousand pounds of mercury is not toxicologically equivalent to a thousand pounds of dioxins.

PANEL MEMBER BLANC: No, what about 50 pounds of dioxin?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: No, we're talking about a great many orders of magnitude difference in terms of the effective concentrations here. We're talking in the dioxin case about being concerned about exposures down to the pico- or fentogram level.

PANEL MEMBER FUCALORO: Then that should show up

in the ratio, right?

SUPERVISING TOXICOLOGIST MARTY: We don't have ambient concentrations and dioxin is just too expensive to monitor.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Yeah, that is an additional --

PANEL MEMBER WITSCHI: I think to bring dioxin down to the -- I mean guinea pigs are not humans and the other way around. We know this. I wouldn't be so sanguine in declaring dioxin the ultimate and most important and toxic agent that's around.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: It's not clear exactly how potent it is in humans and it may be true that humans are less susceptible than some experimental animals, but I think that we are concerned about the levels currently being emitted.

SUPERVISING TOXICOLOGIST MARTY: I think that a very important point that needs to be hammered home is that breast milk is the major source of exposure to a chemical which we know has impacts in infants and children. We are exposed in the first year of life to more than we're ever exposed to in the whole rest of our lifetime. To me that's enough to put it on the list.

PANEL MEMBER BLANC: No, it's not, unless there is air -- I mean --

SUPERVISING TOXICOLOGIST MARTY: There are airborne exposures.

PANEL MEMBER BLANC: No, airborne exposures which are a significant part of the source of the current total exposure. I mean that's why I'm trying to be consistent, I'm trying to understand this in the context of mercury, for example, or arsenic.

SUPERVISING TOXICOLOGIST MARTY: All of the stuff that's in the environment now, the vast majority of it came from airborne exposures.

PANEL MEMBER BLANC: Okay, and where did --

SUPERVISING TOXICOLOGIST MARTY: Okay, we've cut back on that, which is a good thing.

PANEL MEMBER BLANC: I'm not arguing with that.

SUPERVISING TOXICOLOGIST MARTY: But we still have sources and, in fact, both ARB and US EPA are doing a lot of work right now to further characterize the sources of dioxins. So I think it's a very important issue.

There is some modeling work, which unfortunately I don't have in front of me, that was done by the Regional Water Quality Control Board, after the San Francisco Bay was declared impaired because of dioxin contamination of fish, which indicated that the sources of dioxins to the Bay were motor vehicles. That's the primary source of dioxins in the San Francisco Bay.

Now it's a model and so, of course, it's not exactly correct, but it's a pretty interesting indication that airborne exposures are continuing to contaminate the environment and that we already have an environment that is --

PANEL MEMBER BLANC: But couldn't I say exactly the same thing about mercury? Couldn't I say exactly the same thing about mercury and how am I supposed to decide proportionately comparing the 50 pounds per year as in --

SUPERVISING TOXICOLOGIST MARTY: Well, I don't think that the stuff that's in the fish now, the mercury in the fish, it wasn't originally airborne.

PANEL MEMBER BLANC: Yeah, but we're not talking about history, we're talking about what the future --

SUPERVISING TOXICOLOGIST MARTY: I think we're talking about both. I'm talking about both anyway, because I just think that the airborne exposures from dioxin are the most important.

PANEL MEMBER BLANC: Historically.

SUPERVISING TOXICOLOGIST MARTY: And they continue to be even more important because they've cut back on exposures from pulp mills by changing the bleaching process.

PANEL MEMBER FUCALORO: So we are to consider, for example, when we look at exposure levels, we're to consider ingestion if, in fact, it originally was ample?

SUPERVISING TOXICOLOGIST MARTY: Absolutely.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: Can I just intrude a point here?

One of the points that I was making in relation to the sources of current human exposure is that the primary approximate source of the body burden of dioxin, which most people carry around with them, is the food chain.

Now the current airborne exposures are an important contributor to the food contamination. The material turning up in the meat and the dairy products is not coming primarily from the old waste sites, the old river sediments, the old chemical factory sites. It's coming from airborne emissions, because most of the cows grow in areas which are not close to the traditional core contamination sites, which is where a lot of the historical contamination is located.

They're receiving constant input of dioxin into the immediate -- you know the grass, it's landing on the grass, it's --

PANEL MEMBER BLANC: And there is data in this document that support that?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: We have not attempted to duplicate the very considerable amount of work which was done by the US EPA in their recently approved and released dioxin 2000 report, but

we do rely on that to a considerable extent. We have not ourselves had access to such comprehensive studies as what they have reported.

However, this is an area of active of work and, in fact, the Air Board and the various regional -- you know the state board and the regional boards and the water quality boards are working on this.

PANEL MEMBER BLANC: So your argument would be even if there was one pound released per year in California that would be enough to make you want to list it on the top five?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I would be very concerned about minimizing. Given that we are currently into the effect range in terms of what we're exposed to and what we carry around in our bodies, I would be very concerned to reduce the emissions as far as possible, yes.

PANEL MEMBER BLANC: So as long as there were any emissions in California you would put it -- I mean I'm just trying to get a sense again, since we're being asked to do a relative weighting, at least we're being asked to evaluate your relative weighting, I have to be able to understand the logic behind your relative weighting.

SUPERVISING TOXICOLOGIST MARTY: Maybe I can shed a little bit of light. The emissions that are in this table

are stationary source emissions, so that doesn't include all the mobile source emissions of dioxins.

CHAIRPERSON FROINES: Can I interrupt long enough to raise an issue?

I actually think that there are two questions, one of which is absolutely predictable that this discussion on exposure was going to occur, because the exposure question is highly questionable, I think, and so what Paul is doing, I think, had to occur, has to occur.

But the corollary to that is Peter's question, which is that, you know, I think the evidence on carcinogenicity at this point is relatively strong, particularly with respect to soft tissue sarcomas at least. But clearly there seem to be some significant species differences in the toxicity of the dioxins relative to humans so that the exposure question and the differential toxicity between animals and humans, those two are actually coupled.

So when Paul is asking you the question about one pound and you answer yes, that has something to do with both persistence in the environment, but also a perception about the level of toxicity of the compound --

PANEL MEMBER BLANC: Differentially.

CHAIRPERSON FROINES: -- and differential toxicity. So the issues are linked.

I had one question that hopefully might shed some light, but I have a feeling I know the answer. And that is in your diesel document, of course, where you do this thing which I must admit I'm not a great lover of, but I'll live with it, where you list in table one the various toxic air contaminants found in diesel exhaust, you list chlorinated dioxins.

And so the obvious reader of this document has some reason to believe that chlorinated dioxins are released by diesel exhaust and the question then becomes what do we know about that because that's obviously an important issue, and the corollary question would obviously be is there anything in gasoline? But at least with respect to diesel the question is does this constitute a significant release? Does it constitute a negligible release? Is it really no releases?

I don't know the answer to it. And this could represent an important source of dioxin to the degree that there's any being released at all.

(Thereupon a short discussion was held off the record.)

CHAIRPERSON FROINES: The problem is if you list it in your document it's likely to get asked.

PANEL MEMBER FUCALORO: Just again. It's very toxic. I mean you spend some time describing the toxicity,

and I'm not even looking at the differential toxicity at the moment, but just toxic in general.

We're finding it in human beings. We're finding concentration in human beings. And now the question as to what's the original source of it, whether it's airborne at one point or not, that's still undecided, correct? Remember where there are ratios that we were asking before, 50 to one, or something like that, there's no estimate as to what those ratios might be or any guess at what they might be?

SUPERVISING TOXICOLOGIST MARTY: No. We don't have ambient concentration data --

PANEL MEMBER FUCALORO: Is it your guess that most of these materials showing up in human beings are originally airborne?

SUPERVISING TOXICOLOGIST MARTY: Yes.

CHAIRPERSON FROINES: But, Melanie, not wanting -- I don't know the literature here so I'm asking a question out of ignorance. There's a fair amount of herbicide use that's occurred in California over the years too, so that it's not as though there hasn't been a nonairborne source of dioxins into the environment.

I don't know how much herbicide use has been used with dioxin as a contaminant, but that's clearly another source. I don't know, for example, around railroads how much, you know of these compounds have been used to clear

railroad tracks and all the other things that we know that happens with herbicide use.

So I think one has to be a little careful to ascribe it all to airborne releases, given the herbicide use. And I have no idea how much is used over the years.

PANEL MEMBER FUCALORO: You see in some ways the concern here, I mean, is that five slots makes each slot a very dear commodity.

(Laughter.)

PANEL MEMBER FUCALORO: And so if you take up a slot with this, you don't have something else that may also be very adverse to human health.

SUPERVISING TOXICOLOGIST MARTY: I understand that.

CHAIRPERSON FROINES: Let me just say one thing. We spent yesterday with an all day meeting of our particle center with folks from ARB in a very very successful meeting. And one of the things that we learned is that ARB is about to start doing fairly extensive monitoring for dioxins. And so the state is actually in a position where it's going to begin to do monitoring to give us better data on this particular issue.

But it does seem to me, going back to Paul's original thrust of his questions that we are laboring here in terms of the current state of the problem.

SUPERVISING TOXICOLOGIST MARTY: I agree that lots more information needs to be developed in terms of what the sources of dioxins are into the air. But I think it's pretty clear from US EPA's work that currently the majority, over 90 percent of the sources of emissions in to the environment, are coming from the air.

The cows that you eat, that you are eating, which are contaminated with dioxin, they're contaminated because they're eating grass which keeps growing and the input is airborne deposition.

So to me the dioxins that you're getting now in your food are largely from airborne sources with the possible exception of fish near --

CHAIRPERSON FROINES: Yeah, but I get radioactive iodine from China's atom bomb testing from 20 years ago. So what you just said doesn't necessarily carry a lot of water. I mean we get dioxins, airborne, from places all over the world that the winds blow that material over California and so there's deposition in California.

So we have deposition from Japanese dioxin.

SUPERVISING TOXICOLOGIST MARTY: We also have deposition from California generated dioxin. I mean there's no question about that.

CHAIRPERSON FROINES: So, yes, there is airborne exposure to dioxins. Paul's question is, in fact, trying to

get at how much and is it significant. And am I still waiting for somebody to suggest what the -- tell me that either you don't know about diesel or you do and somebody is going to give us a number or what?

SUPERVISING TOXICOLOGIST MARTY: I would have to have Air Board people who are the ones that listed dioxins as being diesel exhaust come and talk about it. I can say one thing that the modeling that I mentioned earlier from the Regional Water Board, that attributed a lot of the dioxins in the Bay to vehicular traffic. They were really talking about truck traffic. But, you know, I don't have that in front of me.

I think it's --

PANEL MEMBER GLANTZ: Do you know anything about diesel versus gasoline?

SUPERVISING TOXICOLOGIST MARTY: I don't, but I'm sure the Air Board does.

PANEL MEMBER GLANTZ: Does anybody from the Air Board, can they comment on that?

CHAIRPERSON FROINES: There's nobody from the Air Board here who's familiar with this area.

PANEL MEMBER BLANC: Well, let me ask, maybe part of the problem is the ellipses in this section of this document. But, you know, it goes right from the toxics inventory to the statement extracted from the EPA document

that 90 percent of dioxin currently coming into the environment comes from airborne sources, which is a statement. But didn't the EPA base that on air monitoring in other states?

I mean I would be more sympathetic if there was a paragraph of data that said airborne dioxin monitoring from 35 states in every state in which it's been done has found ambient levels and these ambient levels range from X to Y, and that would translate into, you know, this kind of -- that would be equivalent to X amount of pounds released in total in California to get to that kind of ambient level.

Because all you have here is the, in italics, the two-sentence statement from the -- I'm not asking you to recapitulate the EPA document, but you're asking us -- this comes back to a recurring issue. You're asking us to make a scientific comment on a document, so I can't make a scientific comment on, you know, here's what the EPA summarized, you know.

I need to have something more than that, especially if it's linked to -- the only hard data it's linked to shows 50 pounds of release.

SUPERVISING TOXICOLOGIST MARTY: Well, let me come back to another argument and that is that the statute requires us to look at not just differential toxicity, but differential exposure. And it's unarguable that a breast

fed infant has much more exposure than a formula fed infant and than an adult.

PANEL MEMBER BLANC: Well, they have to have exposure to something which has -- or are you saying because it's a toxin in general? Okay, but still you have to -- the missing piece is the airborne component piece.

SUPERVISING TOXICOLOGIST MARTY: And what we're arguing there is that the dioxin that's in my body now was largely initially airborne, that's the argument.

PANEL MEMBER BLANC: But where is the data to support that argument other than the statement from the EPA in terms of the current situation?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: There is an extensive report which we cite, which is the US EPA report.

PANEL MEMBER BLANC: But do they have some airborne ambient data?

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: They came to that conclusion on the basis of a combination of measurements and their modeling.

CHAIRPERSON FROINES: I think there are two things to say.

One, as you know, I communicated with Bill Glaze, who was the chair of that committee. And Bill sent me an e-mail back saying that those issues were very controversial.

And I just want to say one thing -- and so I think that the problem for us, as a panel, is that -- and this has come up before and I don't want to make an issue of it, but the citing of somebody else's secondary review doesn't help this Panel with the information.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I think our hope was that we were trying to cite the EPA's primary work of undertaking the measurements and analysis. We may not perhaps have reflected that as completely as we should have done in our citation, but that was the intended reference.

CHAIRPERSON FROINES: But the point is that what Paul is suggesting is that there's inadequate description of what's in the EPA report for him to --

PANEL MEMBER BLANC: Some of it's on the page preceding, I see. So it may be partly a cut and paste issue to an extent.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I'm sure that given a little more time we could do a better job of describing what it is we're referring to.

CHAIRPERSON FROINES: I just want to make -- Melanie obviously feels quite strongly about the breast milk issue and I can understand that, and support her view on it. But I think that the issue of exposure is a question of is there current exposure or anticipated exposure that will

constitute a public health problem in the future?

That's different than saying there has been exposure and now it's in the breast milk. Those are different ways of looking at the problem. And I think that we're really talking about exposure in terms of whether or not it constitutes a current and potentially ongoing public health problem from the standpoint of exposure.

So I think it's not sufficient to say it has occurred in the past and we have to live with it and it does create an ongoing problem in that context, which I would agree with. But the ongoing problem of it being in the air is really one of the issues that we need to worry about.

AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF SALMON: I think there's clearly more work being done and hopefully we will have better detail in the future. But I think the fact that you indicated there's a fair amount of controversy about some of these issues on dioxin. But nonetheless, I think most of the people who are contending nonetheless believe that there is a problem with continuing emissions of dioxins into the air and then getting specifically into the food chain.

This is one of the reasons why both the Air Board and the federal government have been paying so much attention to the issue of backyard trash burning, because this is, I believe, considered to be a substantial source

and one which they feel, you know, needs more attention and better control.

CHAIRPERSON FROINES: Let me ask you a favor here. George and Melanie, let me just ask you a favor. For the moment, the three of you take our place and sit at this table and in other words put yourself in our place.

PANEL MEMBER GLANTZ: Then they could give us a hard time.

(Laughter.)

CHAIRPERSON FROINES: No, wait a second, I'm not joking and we're not giving them a hard time. We're trying to talk carefully through an important issue.

The question is this is a compound or compounds that have been suggested to be in Tier 1, to be the five listed, and we have to make a decision. The decision for us is not whether or not it should be listed in Tier 1. That's really Joan Denton's decision.

The decision that we have to make is is the presentation of the scientific information sufficient for us to approve the document that we have in front of us. That's the decision we have to make.

And so that the level of evidence that's before us is really what's the question that's being raised. And so by putting yourself in our place, help us figure out how can we get to the place where we say, yes, this is sufficient

information or suggest a process by which we can get there on this one, because obviously it's troubling.

So that it seems to me to be the issue that we have to worry about at this point.

PANEL MEMBER BLANC: I think another --

PANEL MEMBER GLANTZ: Let them answer the question.

PANEL MEMBER BLANC: Is there an answer to that? That's not a -- it wasn't a question.

CHAIRPERSON FROINES: I think we should break for lunch and I think we should go away and come back and Melanie and George and Andy can suggest what they think is the best way to think about this in terms of bringing it to closure.

PANEL MEMBER FUCALORO: I lost my appetite knowing there's dioxins --

PANEL MEMBER GLANTZ: I'm a little concerned -- I mean I'm always happy to eat, except not fish, I guess.

(Laughter.)

PANEL MEMBER GLANTZ: Although I used to like fish. But, you know, I think it's important that we come to closure on the findings today and I'm a little worried that we're getting into such a level of detail on everything we're talking about that we're going to be here until midnight, and I mean, I'd just like to raise that. And I

think that, you know, everyone appreciates that you can always ask more questions and raise more issues and I mean it will be interesting to see what people think around the table, which two of these should be thrown out or which should be added.

But I think it's also important to remember that this isn't the end of the process, that, you know, we will come up with the five that the Legislature says we have to come up with by July 1st.

But the law also says you can add to the list as, you know, subsequently. And so I think that some of these things, if people are sufficiently troubled about one chemical or another being in the top five I think it's going to be hard to take two out of this list. Some of these requests for additional information, I think, are things that we can deal with later.

CHAIRPERSON FROINES: But wait a second. I was being very careful in what I said. We don't choose which two chemicals to take out. That's not our job. That's not legislatively mandated for us to do. It is our job to approve or disapprove the documents that we have before us, that's what we do.

Our job is not to make Joan Denton's decision. Joan Denton makes that decision. So I think it's important at this stage for everybody in this panel to recognize that

what we're doing is saying that these documents we approve or disapprove or say go back and start over again, or whatever, but that's what we're doing.

We are not the decision-makers in this law on whether dioxin is Tier 1 or Tier 2.

PANEL MEMBER FUCALORO: In that spirit, John, I just draw your attention to the paragraph on page six, where, frankly maybe it's -- I was very good in reading comprehension, but I'm having a little trouble understanding exactly what's being said here.

It says, "Fortunately between 1987 and 1995 emission of dioxins into the environment has decreased by almost 80 percent from the level reported in the seventies." That's clear. "This decrease is primarily due to decreased emission of dioxin and related compounds into the atmosphere." What is unclear is why was there a reduction in those emissions? Okay, it's not clear.

Then it says, "Because of new regulations promulgated by US EPA in '95 from municipal waste combustors and in '97 from medical waste incinerators, levels of dioxins emitted into the atmosphere from the two sources is expected to result in a greater than 95 percent reduction in dioxin emissions into the air in the United States."

Now 95 percent based upon the seventies or the later number? I mean this is just a matter of clarity. I

mean it's not argument here that I'm trying to make. That is unclear to me and I think that really has to be made clear, exactly why, to repeat, why was this -- what resulted in the reduced emission of dioxins in the period from '87 to '95? And the expectation of a 95 percent reduction, is that an additional 95 percent reduction or is it based on the 1970?

That information must be available.

CHAIRPERSON FROINES: We actually have been over that in a previous meeting and Tony didn't remember it, but we did go over it. At some meeting we have done it.

But I don't want to get into that and I don't want you to answer that question.

If you remember years ago when we did lead, Stan took approximately 36 hours, as far as I could tell, to go through all of his comments on lead. It felt like 36 hours, it was probably two. But whatever it was it went on. And what happened was you then went back and made changes to your document, but in the process we had provisionally accepted your document, even though Stan had just incredible numbers of changes.

My question for you isn't about the substance of the issue, it's about can you go back with this document and develop a discussion of the exposure that would meet the criteria in a sense that Paul's asking about and can you say

that yes, that there is an information, for example, in the EPA document that could be put in. And then the Panel will feel more satisfied with saying, okay, we will approve the issue with respect to -- we'll approve the document with respect to dioxin, given the potential changes. And the Panel has to agree with what I'm suggesting.

I'm suggesting an approach that can move us off dead center, that's all.

I'm using the Stan Glantz model here.

(Thereupon a discussion was held off the record.)

CHAIRPERSON FROINES: Melanie, is that --

SUPERVISING TOXICOLOGIST MARTY: We can do that. We can try to develop the argument.

PANEL MEMBER BLANC: And I guess I want to echo, Stan, something that John alluded to as well in your comment. And that is that I don't want you to have the impression or to give others the impression that we are somehow, quote, "Giving them a hard time," unquote.

PANEL MEMBER GLANTZ: Oh, I was joking.

PANEL MEMBER BLANC: But it's not a good subject to joke on because there was a lot of, you know, morale problems in follow-up to the last meeting, apparently, which, you know, are understandable, but are related to the necessary role that we have to take which can't always be

soft-edged in certain situations. And sometimes the necessity for taking, you know, a somewhat demanding role is necessary in order to fulfill our obligations, at least as I understand them to be.

The reason why we have to be very cautious not to have that veer over into a misinterpretation of giving people a hard time or being difficult or being ornery or being overly aggressive or inappropriately aggressive is because that if we start to stray into that kind of territory we may inadvertently in substance or appearance have the Panel not fulfill its responsibilities fully.

PANEL MEMBER GLANTZ: Well, actually at the risk of delaying lunch, I'd like to actually offer a comment on that, it was a point I wanted to make later, and it was a joke. Just for the record, I was just making a joke here.

But I think if you look at the record and some of the reporting of these meetings and the fact that the OEHHA staff have been questioned very vigorously, we'll say, over the course of the development of this document, I think it's important to actually clarify a couple of things about the way this process on this particular document has run.

First of all, I think that the Panel in being very very vigorous in their questioning of OEHHA as this document has evolved has been totally appropriate. The thing which is different about this one, from most everything else I can

remember from having been on this Panel is that the Legislature adopted a very short deadline for the production and approval of this document. And I think, based on my prior experience on this Panel over a period of many years, this thing got produced in lightning speed and so I think what ended up coming in front of this group wasn't as polished as the typical OEHHA document has been, simply because they didn't have time to go through as many iterations as they normally would before it would come here.

Now I think that was appropriate because I think we should meet the deadline established in the law if we at all can. But I also -- and I think as a result we were seeing and we were commenting on things that were rougher than usually get to the public meetings. And I think that's something that everybody just needs to recognize.

And I think the Panel, because the Panel and the public and the media who have reported on these meetings need to recognize that. I mean I happen to think, notwithstanding the discussion so far today, which I pretty much concur with everything that was said, but the document that we're looking at now, the June draft is far, far, far superior to the previous iterations.

Now does that mean there's -- I mean I think there's a bit more work that needs to be done, but I think in the end we're going to have a document which is up to the

same high quality standards of everything else we've dealt with in here. And I think it's just important to put that on the record.

I was going to give this little speech later, but I think it's very important to put that on the record. And I think the people at OEHHA have been working very very hard on this to try and meet the criticisms and the issues that the Panel has made and that they've imposed on themselves.

And so I just think by the time we finally approve this thing, I think it's going to be up to the usual standards that we work to. And I don't want people to feel that because of the vigorous questioning and vigorous discussion that's occurred, based on earlier drafts of this document, that somehow the final product, as it emerges, is somehow deficient as a result, because I don't think it will be by the time we're done with it and that they're done with it.

CHAIRPERSON FROINES: I think that the comments by Stan and Paul are extremely useful and basically reflect the fact that this Panel has the highest regard and respect for OEHHA historically and currently and will have in the future and so that everybody needs to understand that that's the foundation upon which we operate from, that we have nothing but the highest regard for OEHHA and operate from that vantage point.

And also we're going to be back from lunch at 1:30 and we'll proceed.

PANEL MEMBER BLANC: I think it would be reasonable to say 1:45, so it's a reasonable timeframe, so we're not setting it up to be late in advance. Because I can just tell you even to get the food out of this cafeteria --

PANEL MEMBER FUCALORO: But if he says 1:45 he means exactly 1:45 and not 1:52, okay.

CHAIRPERSON FROINES: 1:40.

(Thereupon the lunch recess was taken.)

AFTERNOON SESSION

SUPERVISING TOXICOLOGIST MARTY: What we're going to do next is go over -- okay, George is telling me that Jim Aguila from the ARB has a comment or two on what they're doing monitor dioxin in California now if you want to hear that.

CHAIRPERSON FROINES: Briefly.

PANEL MEMBER FUCALORO: Seventeen words or less, Jim.

MR. AGUILA: Okay, I'll do my best.

CHAIRPERSON FROINES: We're still interested in knowing about the dioxin levels from diesel.

MR. AGUILA: What I can do is share with you what information the Air Resources Board has on dioxins. And basically, as Melanie indicated, the information that was shared in the report was based on the hotspots data, which again is stationary source information.

We don't have any ambient data at this point, but we have done some testing in connection with the EPA's development of max standards for the refinery catalytic cranking units. And I believe in 1999 the Air Resources Board did some source testing in Chevron and Tosco refineries which indicated that there were low dioxin levels in the beaker gram per thousand barrels --

CHAIRPERSON FROINES: In the oil?

MR. AGUILA: Excuse me?

CHAIRPERSON FROINES: In the oil?

MR. AGUILA: Actually the catalytic cranking unit is a -- it's a unit that produces reformate, which is a high octane blending component for gasoline. And based on that information the Air Resources Board has developed a dioxin testing program, which basically has two parts.

There will be an ambient monitoring component which is scheduled to start in the fall of this year. There will be four sites selected in the Bay Area and four sites in the South Coast as well.

In addition to that there's also going to be another component to that program which is going to look at sources, dioxin sources and source characterization testing. Right now the Air Resources Board is in the process of selecting those sites and they're looking at sites like refineries, medical waste incinerators, hazardous waste cleanup sites. And again that testing will start later this year as well.

There will also be a mobile source component to that, but because there isn't any source test method it's going to take a little bit longer and I believe the timeframe on that will be about 2003.

So basically that's the information we have. We also have some information from a contract study, where they

looked at a single engine diesel engine. And that again showed trace levels of dioxins as well.

CHAIRPERSON FROINES: The question is what's the chlorine source for diesel?

MR. AGUILA: I guess it's speculated that it could be from the engine oil or it's even a component in the crude oil itself. And there is some crude oil that's even transported by tanker truck and you get the sea water in there, so that's a potential source.

CHAIRPERSON FROINES: Thank you very much. We appreciate it very much.

SUPERVISING TOXICOLOGIST MARTY: Okay, what we were planning on doing was giving a very brief overview of five of the chemicals that we've already presented to the panel just as a refresher before your discussion, in preparation for your discussion.

And we also were asked a couple of meetings ago to do a comparison of the information on acrolein and formaldehyde in terms of the guinea pig hyper responsiveness model, so we have that information if you want to hear that too.

CHAIRPERSON FROINES: I think we're particularly interested in the formaldehyde point. I think we're generally familiar with the acrolein, so I wouldn't spend too much time on it. But I think the formaldehyde is the

one for which the evidence is the shakiest, from what we think at this point, but --

SUPERVISING TOXICOLOGIST MARTY: Okay, well we can just skip acrolein and just talk about formaldehyde.

CHAIRPERSON FROINES: It's whatever you think.

PANEL MEMBER GLANTZ: Well, can I just ask a question of the Panel, because I just am worried that we're going to run out of time for the most important part of the discussion.

Of the things in the findings, the draft findings that we've prepared, of the things that are currently listed, you know, in item number eight, which is what we've been calling Tier 2, is there anything there that anybody thinks ought to be moved up? Because if not, then we don't need to further discuss them and we can just go on.

Formaldehyde is in the Tier 1 list right now. But I mean, the things that are listed as ones that we say are concerned but not in the top five, it's arsenic, benzene, carbon disulfide, glycol ethers, manganese, mercury, methylene chloride, methyl bromide, PCBs and vinyl chloride.

So is there any of those that anybody seriously thinks ought to be moved up?

CHAIRPERSON FROINES: Peter.

PANEL MEMBER BLANC: But the caveat is that assuming that they stay in the lower Tier I think that it is

-- I agree the assumption is, however, that there is modifying language that makes it clearer that some of these are of more concern than perhaps others.

PANEL MEMBER GLANTZ: Right. Well, I think that a separate question is do we want to drop any of them from Tier 2. But the question -- I don't think so either, but the question here is so there's nothing that's currently listed as Tier 2 that anybody wants to move up. So I don't think we really need to talk about that at all.

PANEL MEMBER BLANC: That wasn't what she was about to talk about. She was about to --

PANEL MEMBER GLANTZ: Well, yes, she was actually and then there was the question of formaldehyde versus acrolein.

SUPERVISING TOXICOLOGIST MARTY: Stan, right now in the table in the document we still have the old Tier 1, Tier 2.

PANEL MEMBER GLANTZ: I know, I'm talking about the findings.

SUPERVISING TOXICOLOGIST MARTY: Okay, I'm sorry.

PANEL MEMBER GLANTZ: I'm talking about the findings list.

Okay, so having said that, I think formaldehyde -- I agree with John that we should talk about formaldehyde because that's -- I think now we should be talking about

basically -- we've got six of them listed in Tier -- there are six of them listed in the findings and we can only list five, so the real question is what goes.

CHAIRPERSON FROINES: I think for purposes of time, Melanie, you probably should focus on three chemicals or three substances. One being formaldehyde, clearly, the second being changes you've done with respect to PAHs in diesel, seem to be the ones. The acrolein one, I think unless there is any new information or comparative information, you can include it or not include it as you wish.

SUPERVISING TOXICOLOGIST MARTY: Okay.

Well, let's go ahead with formaldehyde and Stan Dawson is going to make a very brief presentation on a synopsis of what we're thinking on formaldehyde.

DR. DAWSON: This is mostly a reminder of what we went through last time and a little bit of a new synthesis.

Formaldehyde was placed in Tier 1 because human data suggests that children are more sensitive than adults to formaldehyde. Studies in children indicate adverse respiratory effects from formaldehyde, concentrations of 13 to 26 ppb compared to a NOAEL of 26 ppb and a LOAEL of 75 ppb for adults. And that's, of course, a continuous equivalent derived from occupational studies in the chronic REL.

And the next point is that data in guinea pigs show increased bronchoreactivity at very low concentrations after eight-hour exposures and extensive exposure data for formaldehyde exist, mean in-door values exceed the chronic REL of 2 ppb by four to 20 times.

Next I have a slide of the concentrations, data furnished by compilation in the Air Resources Board. You can see a number of different locations there and throughout California and averages. The conventional homes and manufactured home samples are throughout California, 11 and 45, and then some US data on public.

The schools was a kind of a special sample the ARB got from the data they could glean at very selected schools, but both northern and southern California, with 26 ppb. These, of course, are all mean values as you can see. And then some values in vehicles.

And finally the outdoor value was 3.6.

PANEL MEMBER WITSCHI: So why would the vehicle values be higher in L. A. than they are in Sacramento?

SUPERVISING TOXICOLOGIST MARTY: That's just the measurements that were made by the Air Board in their in-vehicle study.

PANEL MEMBER FUCALORO: Sacramento has cleaner cars.

(Laughter.)

SUPERVISING TOXICOLOGIST MARTY: You know, there could be a lot of reasons, including congestion on the freeway, you know, that sort of thing, but that's what they got.

PANEL MEMBER WITSCHI: Well, no, but they're much higher.

CHAIRPERSON FROINES: Could you go back to that just for a second?

PANEL MEMBER WITSCHI: Yeah, I mean first of all there must be something in the car that emanates formaldehyde because otherwise it can't be much higher than it is in outdoor air. And so why are the cars in Sacramento different from the ones in Los Angeles?

SUPERVISING TOXICOLOGIST MARTY: I think that if you look at those studies the inside concentrations were not very different than the outside concentrations, and so we're talking about freeways.

PANEL MEMBER FUCALORO: Somebody could have been smoking.

SUPERVISING TOXICOLOGIST MARTY: I don't think -- no, these wouldn't be cigarette smoke because the people driving the cars were ARB employees.

PANEL MEMBER FUCALORO: And you also don't know when they were done, for example, the time of year and also the years apart that they were done.

DR. DAWSON: Actually there's more documentation in the document that you have that gives the footnotes.

Now the four studies that we are relying on for discussing differential effects, the main four human studies, are described here. The first study, the Chris Krzyzanowksi study, is a large study and it's in homes and it has both -- the main thing to point out is it has both children and adults in the study. So there are around 600 adults and 300 children.

And then two of the other three studies are in homes and they are a good deal smaller. And, of course, one of them is at schools.

Now, this is a summary of all these results in these four studies of relevance here. First of all the study is listed on the left and then the objective respiratory effects are listed for each study.

You can see that the bronchial -- well, the two pluses means that that's highly significant, that this is the chronic bronchitis and then asthma and the peak expiratory flow rate are also significant. Note over on the far right-hand column that reported symptoms are nonsignificant. This, of course, is -- these effects are correlated with formaldehyde exposure.

And incidentally they're corrected for various possible confounders.

And then the Garrett study you can see was not significant for asthma but it was for the atopy, as indicated by a skin test. And the Wantke data in schools in Vienna was highly significant for specific formaldehyde response in the RAST test, and that was with a change in schools.

Now also, Wantke should point out, they found a fair amount of correlation among affected children with symptoms, but what was statistically significant was the finding that, with a change in schools, that the symptoms were reduced. And the previous slide showed that the formaldehyde levels had dropped by something over a factor of two.

And finally the Franklin study of very significant changes in the exhaled NO, an indication of lower airway inflammation.

SUPERVISING TOXICOLOGIST MARTY: I think we need to point out that the only study that looked at adults and kids was the Krzyzanowksi study and that for adults there were no significant outcomes that were associated with the formaldehyde bubble.

DR. DAWSON: Right and that's the footnote down at the bottom.

PANEL MEMBER WITSCHI: I have another question. There was also an experiment with formaldehyde and these

were with homes, I think, in Canada which had been insulated with urea-formaldehyde. And there was a fair amount of epidemiologic studies on that one. Do those studies indicate anything about children?

DR. DAWSON: Nothing turned up in our literature search and I looked pretty hard.

PANEL MEMBER WITSCHI: Well, did you look at those studies, I think it was in the Toronto area?

DR. DAWSON: No, I didn't specifically. Our search was four studies that would be relevant for children.

PANEL MEMBER WITSCHI: Well, these were some pretty substantial exposures and there were some, when the whole thing came up, you know, there were some very concerned -- so extensive studies were being done. My point is if those studies do not mention anything explicit in children, whatever is its worth?

PANEL MEMBER BLANC: I was under the impression that you were also going to come back with some of the data on controlled human exposures in terms of persons with and without airway reactivity?

SUPERVISING TOXICOLOGIST MARTY: We actually had that data in our original document. This is with respect to whether or not formaldehyde exacerbates asthma, and that data in adults indicates that you probably have to have presensitisation to fairly high concentrations such as you

would experience occupationally in order to get people to respond to formaldehyde in terms of exacerbating asthma.

PANEL MEMBER BLANC: So there's no experimental evidence that asthmatics are more sensitive to the irritant effects of formaldehyde than non asthmatics in controlled human studies?

SUPERVISING TOXICOLOGIST MARTY: That's right. We have a little bit of animal model information, but --

PANEL MEMBER BLANC: That just shows that if you expose animals to enough formaldehyde you can induce airway responsiveness which is a different question and should be universally true of almost any irritant.

So, to summarize the only study that you have that suggests any preferential effect among children is a single analysis based on home monitors of formaldehyde.

SUPERVISING TOXICOLOGIST MARTY: Right.

PANEL MEMBER BLANC: And other than that you have no other human studies that suggest a preferential effect based on age and you have no animal data that suggest a preferential effect of age?

SUPERVISING TOXICOLOGIST MARTY: We don't have any studies that looked at both kids and adults in the same study, but when you look overall at the studies we have found studies that measured respiratory impacts in kids at fairly concentrations and they were lower than the

concentrations we found when we looked for our chronic REL in adult studies.

Now they're not measuring the same things, so it's real hard --

PANEL MEMBER BLANC: One is measuring the RAST level and in that study one of the things that was impressive was the number of children who had positive specific RAST to formaldehyde, if I understood your synopsis of the study?

SUPERVISING TOXICOLOGIST MARTY: Yes.

PANEL MEMBER BLANC: Is that correct?

SUPERVISING TOXICOLOGIST MARTY: That's what they said.

PANEL MEMBER BLANC: And wasn't it something like 20 percent of the kids had a positive RAST to formaldehyde?

SUPERVISING TOXICOLOGIST MARTY: Yes.

PANEL MEMBER BLANC: I mean there's a biological plausibility issue there. That's such a prevalence of -- for specific sensitivity of formaldehyde it's not been elsewhere reported to my knowledge. Not only that, the whole issue of measuring specific sensitivity to formaldehyde has proved to be quite difficult and I'm not sure that there actually is a reliable RAST method for formaldehyde specific IGE.

I mean you have to do albumin conjugates and it's

very difficult to interpret. It's kind of like the TDI literature only worse, which was why it's been so difficult to even establish convincing occupational specific sensitization to asthma. Even the Burge cases are somewhat problem ridden.

SUPERVISING TOXICOLOGIST MARTY: We agree that that study is kind of standing out there by itself.

PANEL MEMBER BLANC: So, in summary then, you don't have any studies that do a head-on comparison between children and an adult with a comparative exposure except for the study from Arizona?

SUPERVISING TOXICOLOGIST MARTY: Right.

PANEL MEMBER BLANC: And you have negative human data suggesting differential responsiveness among people with airway hyper responsiveness so it's difficult to invoke the argument that it's worse for asthmatics and more children are asthmatic and have smaller airways, therefore it would be worse for children?

SUPERVISING TOXICOLOGIST MARTY: Right. I don't think we can invoke that argument for formaldehyde.

PANEL MEMBER BLANC: So you have good -- on the axis of exposure you have fairly good exposure data. You know that there is a fair amount of exposure out there, but on the preferential childhood sensitivity it's actually this -- I would characterize this evidence as weaker than any of

the others in this category and weaker than many of the ones in the Tier 2, far weaker.

SUPERVISING TOXICOLOGIST MARTY: Yes, I think you can say that.

PANEL MEMBER BLANC: So that having come this far in the process and looking back, I'm looking ahead now to the draft findings, where one of the six is going to go. It seems like to, quote, a new television personality if I were speaking to formaldehyde, "You are the weakest link."

(Laughter.)

PANEL MEMBER BLANC: Would that be a reasonable summary of the data?

SUPERVISING TOXICOLOGIST MARTY: I think that is reasonable. I think it's reasonable and I think it's important to point out that, you know, one of the things we are concerned about with formaldehyde is there's just huge exposure indoor and even outdoor, depending on where you are. And so we felt even though we had just a little bit of evidence that kids might be differentially impacted, we just thought it was an important compound to reckon with.

But I would agree with you, out of all those --

PANEL MEMBER BLANC: I think it was appropriate to reckon with it --

(Laughter.)

PANEL MEMBER BLANC: -- but I think once you've

reckoned with it and if you think about it logically there is a difference -- you know, something, if there's a lot of it out there and it's been fairly well studied, and this is all the evidence there is for it, that's a different issue than some of the other toxins we've talked about where the biological data in experimental systems are very convincing. But where there's no air data and we're simply assuming that there's not an exposure, but we don't know it and it hasn't really been studied very well in humans, so it would have been hard to see the effect even if it's there.

So, you know, if I think of all these things relatively speaking, I'm not quite as concerned about formaldehyde for that reason, because I think something would have appeared. And I think that not only that, but the one study that you have has enough, you know, issues in terms of potential interpretation that to rest as much on it in terms of the differential effect, particularly when they had so much confounding with environmental tobacco smoke. And although they say in the paper that they included that in their predictive model, they don't ever provide the parameter estimates for it.

SUPERVISING TOXICOLOGIST MARTY: That's right.

PANEL MEMBER BLANC: And the description of the statistical methods imply that they took into account the fact that each person is contributing multiple observations

because they have multiple peak flow readings from the same individuals and they used a fixed and random effects model. So I'm assuming that each person was controlled for in terms of how many data points they contributed.

But, basically, what you have is, you know, ten people in the highest exposure category, ten people in the medium and then a hundred in the lower. So a very lot is being driven by a very few people and when they show you the raw data all of the asthma in the children are in children who have ETS exposure and formaldehyde exposure.

So generalizing to formaldehyde alone is a challenge.

SUPERVISING TOXICOLOGIST MARTY: I would agree with that.

DR. DAWSON: I would just say that one saving grace is that the other three studies come in at somewhat similar levels of formaldehyde levels.

PANEL MEMBER BLANC: But they're not looking at a preferential effect.

DR. DAWSON: Yeah, right.

PANEL MEMBER BLANC: And they're not actually looking at the effect that we would tend to think mattered, which is we're not really concerned about formaldehyde sensitization, what we're concerned about is the irritant effect of formaldehyde in children, the nonspecific irritant

effect. Not the fact that 20 percent of the population has become sensitized to formaldehyde, which is not particularly biologically plausible based on other data.

So that really makes me concerned about the Viennese study.

SUPERVISING TOXICOLOGIST MARTY: Uh-huh.

PANEL MEMBER BLANC: I don't think there's any corroborative data from any other epidemiologic study suggesting that 20 percent of children are sensitized to formaldehyde or even one percent of children.

SUPERVISING TOXICOLOGIST MARTY: We didn't find anything.

DR. DAWSON: But I would have thought that the Garrett study which has the skin test in it would be somewhat related to the RAST.

PANEL MEMBER BLANC: It's hard with an irritant to do skin scratch testing, too. I mean it's really -- it's a very difficult compound to study in terms of specific sensitization and very controversial. All the aldehydes are. Glutaraldehydes presented the same problem.

Well, anyway, I think we have consensus. I don't think we need to belabor the point.

SUPERVISING TOXICOLOGIST MARTY: Okay. The other --

DR. DAWSON: Oh, wait, we're not quite finished.

We do have a summary and the first two bullets really just recapitulated what we just said about the Krzyzanowksi study and the other three.

The third bullet I wanted to add that was the studies of guinea pigs show that airways are hyper responsive. And of course there's the simple hyper responsiveness in the sense of Amdur's 1960 studies of airway resistance and compliance at about 350 ppb. And then the Swiecechowksi study, which gets into both that kind of simple resistance and also the resistance as mediated by acetylcholine and then finally the Riedel study, even more recently, which looks a little bit more at the mechanistic aspects.

SUPERVISING TOXICOLOGIST MARTY: We were going to come back to the Panel with a little bit of information on the acrolein versus formaldehyde guinea pig model hyper responsiveness. I'm not sure we need to do that.

Okay.

PANEL MEMBER GLANTZ: Can I just ask a question. Did we just agree to move formaldehyde down to Tier 2?

PANEL MEMBER BLANC: That's what I heard Melanie saying.

PANEL MEMBER GLANTZ: Okay, but I want to see if the Panel thinks that.

PANEL MEMBER FUCALORO: Based upon differential --

or lack of evidence --

PANEL MEMBER GLANTZ: For the reasons that Melanie said, I mean, I agree with doing that. Okay.

CHAIRPERSON FROINES: Paul, somebody said there's a consensus, which since nobody said anything in opposition to it, I took it as being what --

PANEL MEMBER FUCALORO: But that was what the consensus was for, as I understood it, and I agreed and I just repeated what I thought.

CHAIRPERSON FROINES: I'll put it affirmatively. There is a consensus of the Panel that formaldehyde be moved to Tier 2.

PANEL MEMBER BLANC: Well, it may be consistent with what you had stated earlier, the consensus of the Panel is that we accept the revised recommendation of OEHHA that it be moved to Tier 2, because what you're saying is you're going to revise your document to reflect that recommendation, and I think we would find that scientifically valid.

SUPERVISING TOXICOLOGIST MARTY: Right.

CHAIRPERSON FROINES: I'm glad you said that, because I really want every motion that we do is basically around our approval or disapproval or critique of the scientific information presented to us. It's your decision about what you list. We simply review the basis of that

decision and I want to make sure that on every compound or compounds we talk about that that's the criteria that we're using.

PANEL MEMBER GLANTZ: I just want to make one thing clear, though, and this is something we went around and around about in trying to get ready for the meeting. The list, the Tier 1 and Tier 2 lists in the document that was circulated, the June of 2001 draft, are the same lists that have been there for a while. And that table in this report doesn't reflect all of the changes and discussions that have gone forth over the last little while.

SUPERVISING TOXICOLOGIST MARTY: That's correct. It's the original table from back in March.

PANEL MEMBER GLANTZ: Right and, in fact, I had tried to convince them to put it in blank for that reason. But I think consistent with the discussion the findings that were put in front of you reflect, and correct me if I'm wrong, George and Melanie, reflected OEHHA's recommendations at the time they were drafted.

So if the table were to have been redone before this draft document was put forward it would have agreed with the findings.

CHAIRPERSON FROINES: I'm sorry, what table are you looking at?

PANEL MEMBER GLANTZ: Well, I'm looking at the

list of findings. If you look in the document --

SUPERVISING TOXICOLOGIST MARTY: On page 37.

CHAIRPERSON FROINES: But I'm looking at the most current table that's before us which is a table that --

PANEL MEMBER BLANC: Table 1.

CHAIRPERSON FROINES: -- is dated -- is Table 1, that lists proposed TACs that disproportionately impact infants and children, and I think this is the table that we're currently operating under.

PANEL MEMBER GLANTZ: Okay. Well, the findings are consistent with this table.

CHAIRPERSON FROINES: That's correct.

PANEL MEMBER GLANTZ: Right. Melanie, --

CHAIRPERSON FROINES: And that the findings are not consistent with what's in this document.

SUPERVISING TOXICOLOGIST MARTY: That's correct.

PANEL MEMBER GLANTZ: That's right. Okay.

CHAIRPERSON FROINES: For the Panel we are operating under Table 1.

PANEL MEMBER GLANTZ: Okay, which was the separate handout table.

SUPERVISING TOXICOLOGIST MARTY: That's right.

PANEL MEMBER GLANTZ: Okay and the findings were drafted to be consistent with this table.

CHAIRPERSON FROINES: And let me just say that

procedurally speaking in Table 1 formaldehyde was listed as Tier 1 and that based on the discussion with the Panel that OEHHA has decided to move formaldehyde from Tier 1 to Tier 2 and the Panel agrees with that -- that the scientific basis of that decision is consistent with the evaluation of the Panel.

PANEL MEMBER BLANC: And furthermore it appears, Melanie, it appears that if I understand correctly that your current recommendation on the draft Table 1, that in addition to the change that Dr. Froines has just alluded to where the term Tier 2 would replace Tier 1 in the formaldehyde OEHHA recommendation column, you would change the wording on the substances that say possible Tier 1 candidate to Tier 1. And on the one that says probable Tier 2 to simply say Tier 2, and those would be the other modifications to this table that you'd be proposing to us.

SUPERVISING TOXICOLOGIST MARTY: Right, that's correct.

PANEL MEMBER BLANC: And is it your proposal then that this table, which is currently labeled Table 1, would essentially be inserted into the document and replace the current table that's on page 37 of the draft document?

SUPERVISING TOXICOLOGIST MARTY: That's right.

CHAIRPERSON FROINES: Now, Melanie, one further question. I don't know if we're at a place where you are

making a new recommendation with respect to acrolein?

SUPERVISING TOXICOLOGIST MARTY: Yes, well, when I put that table together for the Panel we wanted -- OEHHA wanted to hear the discussion today and to get a chance to gather up all of the Panel's comments before we formally made a new table with these new proposals. And I'm sorry, I don't have the table in front of me, but I believe I put for acrolein, potential for Tier 1.

PANEL MEMBER BLANC: That's why I used the wording I just did, that would take that into account.

CHAIRPERSON FROINES: Right. And so what I'm saying is that it seems to me at this point that, based on the evidence that the Panel has reviewed with respect to acrolein, I think that, based on the review of that evidence the Panel is comfortable or would conclude that a decision to move it to Tier 1 would be appropriate.

SUPERVISING TOXICOLOGIST MARTY: Okay.

PANEL MEMBER BLANC: And the same is true for the other one that is worded possible Tier 1, which is diesel exhaust particulate, and it's also true for the one that says probable Tier 2, which is a change, which is benzene. In other words what you're proposing now is that the word probable be deleted, the word possible candidate be deleted and it simply say Tier 1 and Tier 2 respectively, and formaldehyde where the actual Tier is changed.

CHAIRPERSON FROINES: Well, we haven't gotten to diesel yet, so let's --

SUPERVISING TOXICOLOGIST MARTY: Okay.

PANEL MEMBER FUCALORO: But that's in anticipation of what's going to happen, because now we have five substances in Tier 1.

CHAIRPERSON FROINES: But I don't want to start making changes before we've heard the presentation on the chemical.

SUPERVISING TOXICOLOGIST MARTY: Okay.

PANEL MEMBER BLANC: Are we anticipating another presentation on diesel?

SUPERVISING TOXICOLOGIST MARTY: We gave a presentation at the last meeting. We do have a quick overview presentation if you want to see it again just to remind people of where we were.

CHAIRPERSON FROINES: I think that the important issue that came up at the last meeting was around the asthma and the adjuvancy if there is such a word, adjuvancy, the adjuvant effects of diesel. And we requested a considerable improvement in the literature associated with diesel to the degree that you felt that was appropriate. And so what we need is a review and a discussion of where you've come to on that issue, because you've obviously evaluated a lot of new information and whatever your perspective, I think it's

important for us to hear what that perspective is.

SUPERVISING TOXICOLOGIST MARTY: Okay.

We did consider that diesel exhaust particulate, that there was a lot of evidence that diesel exhaust particulate enhances allergic response, and this is in both animal models and in humans. And it's by internasal installation as well as by inhalation.

So we did have that argument in the original draft of the document and what we did was we expanded discussion of those studies in this draft.

So I think we still think that that's a very important issue for diesel and it's probably the strongest piece of evidence for diesel because enhancement of allergic response can mean exacerbation of allergic airway disease, including asthma -- I'm getting ahead of myself.

So we initially suggested diesel exhaust be in Tier 2 because of the enhancement of allergic response, evidence of respiratory health impacts in traffic studies, which we reviewed at the last meeting, and because diesel exhaust particulate is a component of PM10 and PM10 has a number of studies associating it with exacerbation of asthma in infant and actually child morbidity and mortality, including respiratory symptomology. And in addition diesel exhaust contains polycyclic aromatic hydrocarbons which we are concerned about and are a candidate for Tier 1.

And on top of that, in terms of dosimetry children in the same environment as adults will receive a higher particle dose per lung surface area because of their larger breathing rates and smaller airways and then the dynamics of deposition.

There are probably 60 or 70 studies now looking at co-exposure to diesel exhaust particulate, along with allergen, and a number of parameters have been measured that indicate the release of pro-inflammatory --

CHAIRPERSON FROINES: Excuse me, just a second. Okay.

SUPERVISING TOXICOLOGIST MARTY: So there have been a number of studies and these are studies in people as well as in animals, showing that when you co-expose a person by internasal installation or an animal to allergen and to diesel exhaust particulate that you could enhance the animal's or the person's response to the allergen. And this has been measured in a number of ways, including looking at enhanced IgE and IgG response to the aeroallergen and increases in pro-inflammatory cytokines and chemokines in lavage fluid.

There's also studies that have been done that have shown potentiation of histamine release upon exposure to the allergen in the presence of diesel exhaust particulate relative to just exposure to the allergen itself. That's

what all of these things are relative to.

And all of these things have implications for exacerbating allergic airway disease including asthma. In addition diesel exhaust particulate enhances the development of new allergy and this has been shown in an animal model. And this has implications for increasing asthma prevalence.

We also went over some of the traffic studies that have correlated increased respiratory symptoms and decreased lung function in kids to track traffic density to measurements of fine particulate soot in several cross sectional studies. And in one of those studies it appears that the children in the household were more sensitive to the decrements in lung function than the adults.

Diesel is a source of PM10. There are numerous studies associating PM10 with exacerbation of asthma. There's a half dozen studies or so looking at neonatal infant and child mortality and found in association with both short-term acute episodes as well as longer term exposures to PM10.

There have been studies associating decreased lung function in kids with PM10 exposure and then again children experience higher particle loads per lung surface area than adults breathing in the same environment.

Diesel exhaust particulate contains PAHs and nitro-PAHs. These PAHs have been associated with

developmental toxicity in a number of studies, including reduced birth weight and dismorphogenesis.

There is demonstrations of increased susceptibility of the fetus or neonate to the genotoxicity of PAHs. Insofar as we know PAHs probably contribute to the carcinogenicity of diesel exhaust and the PAHs on the diesel exhaust are bio-available.

This is just a quick slide on exposures. The first bullet is our chronic REL of five micrograms diesel exhaust particulate per cubic meter of air. The ambient air is somewhere around two micrograms per cubic meter, a statewide average.

The ARB has measurements that show near a freeway they got up to ten micrograms per cubic meter and then in their in-vehicle exposures they got three to twenty-three micrograms or so of diesel exhaust particulate per cubic meter as measured by elemental carbon.

So, the point is there are exposures and some of the exposures are higher than our chronic REL.

PANEL MEMBER BLANC: So in terms of modifications during your previous presentation there's even more evidence than previously cited in terms of the adjuvant effect or the possible role of diesel particulate in sensitization --

SUPERVISING TOXICOLOGIST MARTY: Yes.

PANEL MEMBER BLANC: -- and a potential for

inducing asthma?

SUPERVISING TOXICOLOGIST MARTY: Yes.

PANEL MEMBER BLANC: And did you find any additional information on exacerbation of preexisting asthma or that basically is the same data that you had before?

SUPERVISING TOXICOLOGIST MARTY: That's basically the same data that we had before.

PANEL MEMBER BLANC: I think one other thing that the record should indicate is that there certainly has been discussion today that, not only polycyclic aromatic hydrocarbons that are recommended for Tier 1, but also dioxins may be present in diesel exhaust. I understand there's a bid questionmark with that, but since the issue was raised and then confirmed by the later speaker, I think that that has to be taken into note, particularly given how strongly you were on record that any reducible exposure was important even if a small percentage.

Another issue, as a minor modification of the document, although it may already be in there, would be in terms of preferential childhood exposure if it's assumed that heavy density roadways are a significant hotspot, as it were, for diesel particulate I think the argument could be elucidated that because lower socio-economic strata are associated with living areas closer to freeways and because the number of children per thousand population are greater

in poorer areas that, in fact, disproportionately in California, children would tend to live nearer to freeways than adults, as a percent of the adult population compared to the percent of childhood population. If that argument makes -- I don't know if I've --

SUPERVISING TOXICOLOGIST MARTY: Yeah, that makes a certain amount of sense. I think I might add to that that the incidence of asthma in African-American kids is higher than in white kids and they tend to be in a lower level generally.

PANEL MEMBER BLANC: But that would be an ideologic leap, but clearly you know -- I think the data, the census data allow you to say unequivocally that more children live near high density roadways. I mean I don't have the data at my fingertips, but I think those data should be available.

SUPERVISING TOXICOLOGIST MARTY: We can look for the data.

PANEL MEMBER FUCALORO: Based upon the average number of children per thousand in poorer groups --

PANEL MEMBER BLANC: So, in summary, therefore, you would say that the biological plausibility, the reproducibility and the strength of the association are present on the scientific side and on the exposure side there is very clearcut exposure to the total population and

some evidence, indeed, of higher exposure and higher delivered dose to children?

SUPERVISING TOXICOLOGIST MARTY: Yes.

CHAIRPERSON FROINES: Peter? Stan?

PANEL MEMBER GLANTZ: No, I agree with that and I looked over the rewritten section in the report on diesel and thought it was much better than when we last discussed it. And these issues -- some of these things you just raised Paul are sort of -- aren't in there, but the key points from the presentation are cleared out much -- or spelled out much more clearly than they were in the previous draft.

CHAIRPERSON FROINES: Tony?

PANEL MEMBER FUCALORO: No, that's fine.

CHAIRPERSON FROINES: I'll be the negative side of this comment.

There are still references missing, but I'm not going to -- but you've got a lot of references, so I'm not going to raise that further.

PANEL MEMBER BLANC: They would only tend to make the argument stronger in your opinion?

CHAIRPERSON FROINES: Yeah.

But there are some issues that I think I just want to point out that I have trouble with. First, I really do support, because it's research that we're doing, the points

about IgE and IgG and other responses, so I would certainly support that.

I still, and at the last meeting the entire Panel rejected my point of view and so I'm a minority here, but I really don't agree with this notion that argues that because diesel is a constituent of PM10, therefore, diesel must be causally related to the same effects that are seen in PM10.

I think that one can make that argument. I think that that argument is too speculative for me. I can't accept it and so that one I have trouble with.

And I just want to mention here. It says "Ostro, et al, 1996." Now in the references that is an Ostro reference to a -- that --

PANEL MEMBER BLANC: I thought there were two Ostros.

CHAIRPERSON FROINES: Pardon me, that Ostro, 1996 is not in the references. It's not there.

Secondly Ostro, et al, 1996, for which the reference is missing in a mortality PM time series study in Santiago, Chile cites Sandoval, 1985. Sandoval reference is missing. It's also not there.

Diesel vehicles account for 87 percent of black smoke emissions in London," Quarg, 1993. Is there an epidemiologic study that that relates to, because I didn't find it?

You don't have to respond, this is stuff that you can follow up on.

"Ostro, 1995, found significant associations between PM10 and asthma symptoms." That's a proceedings, it's not a peer reviewed article. We generally --

PANEL MEMBER BLANC: You may not be absolutely correct on that, because that's published in "Inhalational Toxicology" and often proceedings in journals are, indeed, peer reviewed, so I wouldn't be too --

CHAIRPERSON FROINES: I know that proceedings and I know that conference.

PANEL MEMBER BLANC: And it was never peer reviewed?

CHAIRPERSON FROINES: And I don't believe it was peer reviewed, no. It's Bob Fallon's conference at U. C. Irvine.

Then there is an Ostro 2001 cited for which there is no reference to be found. So that section needs some additional cleaning up.

SUPERVISING TOXICOLOGIST MARTY: Okay, my apologies.

CHAIRPERSON FROINES: It's all right, it's all right, people make mistakes.

Nobody on this Panel has ever made a mistake but --

PANEL MEMBER BLANC: Other people might.

(Laughter.)

CHAIRPERSON FROINES: "In a large study in 12 southern California communities, asthma, bronchitis," so on and so forth, and "were associated with PM10 pollution. Though because of pollutant covariation these effects could not be ascribed exclusively to PM," and you quote John Peters' studies.

Now I think it's very important to emphasize that the John Peters study demonstrates that there are changes in lung function growth. They do not argue that there are changes in lung function, as your document proscribes. And it's lung function growth and it's important to look at the data, not only in terms of the measures of FEV1, but there's also data now available on MMEF on lung functions that look at airways and those results are somewhat different.

But the point I want to make is that what John Peters shows is that there are chronic effects of lung growth in Southern California, in the 12 Southern California communities. He does not demonstrate a causal relationship between those chronic effects in children and any pollutant whatsoever. He shows that there are relationships with PM10, with PM2.5, with acid, with NOX and he shows no effect with ozone, but they also have some data showing some ozone effects.

So that what you have -- and clearly all these measurements are correlated with one another, so at this point what you can say is that children are adversely affected, in terms of their lung function growth, by air pollution and we don't know what causes it at this point.

So to associate it with PM10 is just not on. It's just not a conclusion, and if you ask John Peters, he would not make that conclusion anymore than I would make that conclusion.

So that I think it's not appropriate to suggest that that one finding, where they do find -- they draw a regression line and they see lung function changes, lung function growth changes with PM10, to then ascribe that to being a causal relationship.

PANEL MEMBER FUCALORO: Why, because you don't know if it's diesel or PM10?

CHAIRPERSON FROINES: You don't have any idea what's causing those lung function growth changes. You don't know if it's nitric oxides, nitric oxides with CO, nitric oxides with acid, nitric oxides --

PANEL MEMBER FUCALORO: So they haven't --

CHAIRPERSON FROINES: No, they don't know.

PANEL MEMBER BLANC: So, John, I just want to try to convert your comments into sort of guidance and see if I understand what you're saying.

I think what I hear you saying is that there are so many areas of the diesel story which are so solid in terms of the preponderance of scientific evidence that in the area of PM10 it would be prudent to emphasize the caveats in that particular portion of the argument, because the case does not stand on that. It's an interesting area that warrants further data and as long as you couch it as being speculative, it's certainly worth alluding to and if the document didn't comment on PM10 and some of the PM10 data, it would be deficient.

But it should simply be perhaps highlighted as, you know, -- although of a speculative nature it is important to note that there have been associations with PM10. Two important pieces we don't have is the diesel contribution to PM10, the important factor in this. And secondly, to a certain extent, the causal association between PM10 and some of these outcomes remains to be established, although there is certainly a great deal of concern that that is the -- am I summarizing your comments?

CHAIRPERSON FROINES: Yeah, I would say that the -- my comments are about evidence. They're not subjective. I think that there is significant evidence of enhanced allergic responses and I would certainly agree with you and I think your document has improved, especially in dealing with that area.

I think the Brunekreef studies and others on -- the traffic studies that are in the literature also support those conclusions.

Certainly the PAH, -- the fact that diesel contains PAHs is also evidence that has relevance. And the higher particle dose per lung in children also has relevance.

I think that the issue of it being a compounded PM10 and PM10 effects, we have an entire particle center that's studying these kinds of issues at this point and I suspect that diesel, as a component of PM10 may have effects on asthma and other respiratory changes. But I think that in the current document that it is more speculative than I think the evidence would allow for.

PANEL MEMBER BLANC: Where it's not explicit enough about those parts of it which are speculative is more what -- you're not saying that it's irrelevant, you're just saying it should be couched appropriately?

CHAIRPERSON FROINES: That's right. And I think that they did, by suggesting that there is auto-correlation they do, sort of, acknowledge it. But I think that one could take that a step further.

SUPERVISING TOXICOLOGIST MARTY: Okay.

PANEL MEMBER BLANC: And also, you know, as the evidence begins to emerge that PM2.5 is even more important

that's only going to weigh the diesel argument more strongly, isn't it? Because isn't the diesel particulate even a bigger proportion of the PM2.5?

SUPERVISING TOXICOLOGIST MARTY: Yes, it is.

CHAIRPERSON FROINES: Well some of us even think that the ultrafine fraction is even more important.

PANEL MEMBER BLANC: And won't that even more weight towards diesel?

CHAIRPERSON FROINES: Well, but it's -- having spent two days at a gasoline conference, the issues are very complicated.

PANEL MEMBER BLANC: I understand, but as long as it's put in the right context I think it's -- it shouldn't be not mentioned, it should just be put in context.

PANEL MEMBER WITSCHI: Just out of curiosity, John, how did John Peters hope, in view of the fact that he uses lung growth, which is an integrated measurement over time caused by integrated exposure, how did he ever hope to attribute anything to any part of this mixture, if you are dealing with internal exposure?

CHAIRPERSON FROINES: Well, my view of John Peters' study -- I'm a wild enthusiast for John Peters' study. I think it represents one of the most important studies that's ever been done, precisely because it shows long-term effects, chronic effects on lung function growth

in children.

And I think showing the health outcome is absolutely crucial and important. I think it also demonstrates very clearly how difficult it is to then assign, however, those effects to a specific pollutant.

I mean here we are dealing with 10,000 chemicals and obviously how we sort that out is very difficult. I don't think you can sort out the answer to that question using epidemiology. I think the only way you can do it is through hypothesis based studies in the world of toxicology. It's the only thing that gives you a sufficient laser or scalpel to test hypotheses, because epidemiologic studies, as you know, tend to be broad in nature and are not very precise in terms of establishing causal relationships.

Now if you're lucky enough the way Stan is you can demonstrate cigarette smoke can do it, but it's -- I'm finished.

PANEL MEMBER BLANC: All right. Thanks.

Now I think this would be, maybe timing-wise, just a clarification on the form that you see the document taking in terms of the written basis for the Tier 2 substances that were presented orally today, but for which we --

PANEL MEMBER GLANTZ: Can I just raise one thing before you get on to that?

I just want to absolutely for the record make sure

that we've nailed down the lists. Then we can go on to talk about the document.

CHAIRPERSON FROINES: No, we're not ready for that.

PANEL MEMBER GLANTZ: Okay.

CHAIRPERSON FROINES: I appreciate both of your attempts to move this along, but right now we have a very important issue we have to address before we get to this.

PANEL MEMBER GLANTZ: Okay.

CHAIRPERSON FROINES: And that is that these documents that we've received, including these six documents, this document and the table, Table 1, we've all seen. The public, however, has had a limited timeframe to see it and the public has not been given the opportunity yet to make comments about the quality and nature of these documents. And because of that there's been no response either from OEHHA about the public comments, so what we need right now is to learn as a legal procedural matter how we then proceed from here.

PANEL MEMBER FUCALORO: I just keep losing sight of the road map here. Once we hear from this, what do we do then?

PANEL MEMBER GLANTZ: Well, let's hear it first.

CHAIRPERSON FROINES: I'll tell you what our --

PANEL MEMBER GLANTZ: Let her just tell us.

PANEL MEMBER FUCALORO: I mean in other words it's uncertain depending upon what's going to be said now?

PANEL MEMBER GLANTZ: No.

CHAIRPERSON FROINES: No. What she's going to tell us is going to be procedurally how to deal with the question of public input. And I could tell you what I think we should do, but I think that we should get an official position.

PANEL MEMBER BLANC: Well, let's hear the presentation.

MS. HECK: Thank you. Colleen Heck for OEHHA.

What I would envision happening, procedurally from here, would be that, as you pointed out from the Chair, that there has been no formal public comment period on the revised document.

In the spirit of the statute and just even a more conservative interpretation of the statute, I think it would be appropriate if there would be a comment period at this time on the revised document. But there's been, in effect, revisions to the revised document during the course of the meeting, so I think what would work best would be if we were to capture the revisions taken orally today in writing, in very quick order, circulate those for public comment, ending, we think what would be feasible would be July 6th would be the proposed close of the public comment period.

We would do responses to comments and then send those to the Panel and envision another meeting at which there were a firm list of five being put to the Panel for its approval for its findings and then formal findings made at that time and then the work on this program matter for this portion of it, this first effort would be done.

PANEL MEMBER BLANC: How does that impact the July 1st deadline?

MS. HECK: It concedes that the date will be missed.

PANEL MEMBER GLANTZ: Well, I have a problem with that, because the law says July 1st and I don't see how -- I mean first of all I agree -- well, there's a couple of things you said that I find very problematic.

Okay, the first is I don't see how a lawyer can get up here and advise the Panel to ignore a deadline set by the Legislature in law.

MR. HECK: I didn't advise the Panel to ignore the deadline.

PANEL MEMBER GLANTZ: Okay, well, but that's the effect that it would have.

The second thing, which I think is more problematic is the implication that because there are some changes to the report that were going to be made as a result of the discussion at the meeting, that that report should go

out for public comment. Because, in fact, every report we've ever dealt with since I've been on this Panel was revised as a result of the final discussion by the SRP at the meeting. And I would hate to establish the precedent that any time we change the document at a meeting where we've made findings it had to then go out for public comment again, because we will then create an infinite loop.

Now having said that -- so I take quite strong objection to that. Having said that, I do think it's reasonable to, after integrating all of this stuff, allow public comment on the revised document. Not because of what happened at his meeting, but because of the many changes that have been made as a result of the last few meetings.

But what I would propose we do in order to respect what the Legislature has said is I would propose that we do adopt the findings today. And then if there is a procedure that the SRP has for amending these things and if material is produced during this public comment period, which leads the Panel to reconsider the findings, then we would just reconsider them in accordance with our standard procedures.

You know, given that these compounds are already all identified as toxic air contaminants and have been kicked around quite a lot, I mean I'd be very surprised if any radical new information becomes available, but I do think people ought to have an opportunity, you know, to look

at the document and in what is essentially a final form.

But that anyway is the document that we'd be moving forward to the Director of OEHHA. So I'm just very reluctant to just blow off -- I mean I realize that the creation of this deadline, as I said before lunch, has made the process more difficult and has led to more preliminary versions of this document being released and discussed than would normally be the case, but I mean I think we need to take an action consistent with the direction we received from the Legislature.

MS. HECK: Let me just briefly respond.

I did not mean to imply or set a precedent that every revision triggers another public comment period. I was only suggesting that in the sake of efficiency, since changes were, in effect, generated today, they would be rolled into the revisions that we would otherwise be making, so let me clarify that, and thank you for that clarification.

The other thing, I neglected to say and I had taken the liberty of making some proposed edits to your draft findings, that they, in fact, if you chose to go forward today, that you go ahead and do that, but make it very clear that they're subject to change if necessary or appropriate after the comment period, that they be somehow cast as provisional or subject to finalization at a later

date. I neglected to mention that.

PANEL MEMBER GLANTZ: Okay, I don't have a problem with that.

MS. HECK: Then lastly, there would just need to be clear at some point that this is an OEHHA list, as Dr. Froines has mentioned consistently throughout today's proceedings, that the Panel is making findings on as opposed to the, you know, the Panel's product, if you will.

So with all of those caveats I think we have a road map that we could follow.

CHAIRPERSON FROINES: I need to step in here. I think that these are all highly relevant comments. I would suggest that what the panel does today is to -- let me go back one step.

I have a problem with accepting these findings. I will not vote to accept the findings, because I haven't read them yet.

PANEL MEMBER FUCALORO: Because, I'm sorry?

CHAIRPERSON FROINES: Because I haven't read them. I think it would be inappropriate for me to vote for findings that I haven't read yet. I don't know if Paul or Peter or Tony have read them. I suspect that any reading that's been done has been at least cursory and I think that this Panel on such an important issue should not say we're going to accept these findings at the current state of their

preparation.

So I'm not ready to do that, Stan. That's not where I'm at, because I haven't read them and I'm not going to put my name on something that I haven't read yet.

Secondly, I think, though, that the panel can vote to provisionally accept the documents that we have before us, including Table 1, pending a review by the public and pending comments from OEHHA. And that if there is additional new information then the Panel will reconsider its views of the document. But pending no additional information that changes the views of the Panel that the Panel will then finalize its provisional decision, but the Panel won't reach a final decision until we have actually seen the comments and the responses from the public. But that we can vote, provisionally for the draft as it currently exists in order to -- so that the Director of OEHHA --

PANEL MEMBER GLANTZ: Which draft? This draft?

CHAIRPERSON FROINES: These drafts that we've received, so that the Director of OEHHA is put on notice that the Panel has provisionally accepted the documents as they're currently written. And then at a later time this month we will finalize and vote on the findings, the final findings and send them forward to Director Denton, accordingly.

So that's my current view of how we should proceed. I think this Panel should never adopt, make its final determination on the quality of these documents prior to having public input to them, because will raise important issues and we should -- are obligated to review that.

So I think that we can, provisionally, accept them with a final conclusion occurring towards the end of July.

PANEL MEMBER BLANC: Can I just modify your comment? I think what we have to be referring to in our preliminary approval would be of the data presented today, not of the documents presented today. Because we have an important asymmetry and this is what I was trying to get at and it's appropriate for counsel to comment on this.

I believe that the final document, however it comes out and in whatever timetable, has to treat all of the Tier 2 recommendations equally in terms of a textual approach. I am sensitive to what Stan said about the time demands. Therefore I think within the immediate needs of your document what I would suggest is that for the existing summaries of substances which you are now recommending be in Tier 2, you reduce those summaries to two to three pages only, and that for the approximately five substances for which you do not, at this time, have written summaries, but only the slide presentation text, that you draft two- to three-page summaries of those. And that the document that

you circulate to the public have such text summaries for all of the Tier 2 substances, otherwise we would be in the position of having text supporting some of the decision and text being absent for some of the other.

PANEL MEMBER FUCALORO: And, Paul, you would suggest that they pay particular attention to the issues earlier today regarding why a particular substance ended up in Tier 2, again, whether they affected children more or --

PANEL MEMBER BLANC: I think it would be useful to have a summary paragraph at the end of each of those brief discussions, which says that the evidence appears to be quite strong in terms of childhood susceptibility based on reproducibility, strength of the association and biological plausibility, however exposure data are largely absent, although we do have some concerns about hotspots.

Actually I think such a summary at the end of the ones that you also cite would be useful as well.

PANEL MEMBER FUCALORO: Really useful for the future I think.

CHAIRPERSON FROINES: I think it's important to --

MS. HECK: I think those are all very helpful comments.

CHAIRPERSON FROINES: I think it's important to also pay close attention to the writing of the manganese document, because the one thing -- it was the one chemical

that emerged today for which the evidence, if it wasn't for the exposure data, it would clearly be on the first list of five, and so I think it's important to highlight that.

The second thing is I want to disagree just very slightly with one comment, which is I made some comments about PM10, but those changes are almost cosmetic, because they refer to references, although I think I also made a more substantive argument about the nature of the PM10 argument.

But aside from that, I don't think there were that many changes that were proposed by the Panel today, and so I think that the issue of what goes out for public review is your decision to make. I would try and send out a revised document with the diesel argument changed slightly, but I think that some of the other documents I think are already out in the public.

PANEL MEMBER BLANC: But the brief summaries of all of the Tier 2 have to be in there and they don't currently exist.

PANEL MEMBER GLANTZ: Yeah, but I'd like to just, you know, I mean I think what you're suggesting, Paul, in terms of symmetry would be ideal.

PANEL MEMBER BLANC: I think it's necessary, I don't think it's ideal. I think for it to be a scientifically valid --

PANEL MEMBER GLANTZ: I don't see what's to be gained.

PANEL MEMBER BLANC: Because how am I supposed to comment on a nonexisting document?

PANEL MEMBER GLANTZ: No, no, I'm not, wait, wait, wait. I'm not disagreeing with what you said about the material to be added.

PANEL MEMBER BLANC: Yes.

PANEL MEMBER GLANTZ: But I don't see where we gain, you know, anything of substance by going through and trying to rewrite to shorten the stuff that's already there just in the interest of esthetics, because then what -- first of all the resources available to OEHHA to do all of this are limited by the number of hours in the day.

I think it's very important that this be moved expeditiously and if you start whacking stuff out of those sections which people are already comfortable with then you raise the specter of someone getting mad that something was deleted. And I frankly don't see what you lose by providing more rather than less information.

PANEL MEMBER BLANC: Then I'll make clear why I think there's something to be -- why it's not just cosmetic. And that is because it gives the impression that you've actually given more attention to some chemicals than you have to others. And I think it's very important that the

written record be consistent and my impression from Melanie was that, in fact, such a synopsis or summary of the existing five other longer documents was not a burden that would be excessive.

PANEL MEMBER FUCALORO: Well, that's the question. Stan, I recognize your concern, but they're the ones that actually have to do it and they know what personnel they can devote to it. Does this seem to be a very onerous task that's being asked of you?

CHAIRPERSON FROINES: Do you think we'll get a single answer here?

PANEL MEMBER FUCALORO: Well, take the time you need.

PANEL MEMBER BLANC: Della Street is talking to Perry Mason, the question is which is which.

(Laughter.)

SUPERVISING TOXICOLOGIST MARTY: I'm looking at the length of the Tier 2 summaries that we already have and it's variable. Some of them are pretty short already. And if you say three to four pages, excluding references, we're actually almost there for some of them.

PANEL MEMBER BLANC: Okay.

SUPERVISING TOXICOLOGIST MARTY: I think in terms of workload, yeah, you know, it's another thing we've got to do before we get the document out the door and George is

already mad at me for not giving him enough time to read through this stuff. But, you know, I don't want to spend a whole lot of time hacking at them, but I think we can do it.

And also in terms of the chemicals that we talked about today, we actually already had very early drafts on those which we didn't take through the process, so we already have something written for those. We have to fix it a little bit, but I think I can get them all to approximately, you know, plus or minus however much data there is for each one, ten pages.

CHAIRPERSON FROINES: The answer we got was yes. Thank you very much. That's great.

And George is nodding his head for the --

PANEL MEMBER FUCALORO: He's in a coma.

(Laughter.)

SUPERVISING TOXICOLOGIST MARTY: I'm looking to see if staff is drawing any weapons.

(Laughter.)

CHAIRPERSON FROINES: Now I think we need a motion to provisionally accept the data. You make the motion since you, I think, stated it better than I did.

SUPERVISING TOXICOLOGIST MARTY: John, we were -- did you want us to talk more about PAHs or were you guys okay with that?

You're okay with that.

CHAIRPERSON FROINES: I don't think so. I think that we're prepared to accept the PAHs. If you want to convince us not to, you can do that, but I think you're heading in the wrong direction.

SUPERVISING TOXICOLOGIST MARTY: Okay.

CHAIRPERSON FROINES: Let me say it more explicitly. I think that the evidence that's been presented on PAHs in the past is sufficient in terms of the Panel's review for the Panel to accept the data that was contained within the documents.

PANEL MEMBER GLANTZ: And naphthalene.

CHAIRPERSON FROINES: Including naphthalene.

PANEL MEMBER BLANC: I would like to move that the Panel provisionally accept the data presented today by OEHHA in text and in slide presentation and specifically that we accept the modified draft Table 1 as presented with the noted deletions of the words "possible candidate" or "probable" and the substitution of the words Tier 2 for Tier 1 for formaldehyde.

PANEL MEMBER GLANTZ: Second.

MS. HECK: Was there any mention of diesel moving from Tier 2 to Tier 1?

PANEL MEMBER BLANC: I just covered that. I said -- it was already said possible Tier 1, so by -- it said possible Tier 1 candidate, so by deleting the words

possible and candidate it becomes Tier 1.

CHAIRPERSON FROINES: Is there any discussion?

PANEL MEMBER GLANTZ: Could I just, again to avoid any possible confusion, let me just read what I understand the list to be.

For Tier 1 would be lead, acrolein, dioxins, polycyclic aromatic hydrocarbons, and diesel exhaust particulate. And Tier 2 would be formaldehyde, arsenic, benzene, carbon disulfide, glycol ethers, manganese, mercury, methylene chloride, methyl bromide, PCBs and vinyl chloride.

CHAIRPERSON FROINES: Nonplanar PCBs.

PANEL MEMBER GLANTZ: Okay.

PANEL MEMBER BLANC: Yes, as a point of information, that is consistent with the resolution as put forward.

PANEL MEMBER GLANTZ: I second the motion.

CHAIRPERSON FROINES: All in favor?

(Ayes.)

CHAIRPERSON FROINES: Opposed?

PANEL MEMBER BLANC: The minutes should show that it was unanimous.

Now I'd like to make a suggestion in light of the resolution that was just adopted that the Chair work on draft findings, tentatively consistent with the thrust of

that resolution and circulate it for comment to the Panel Members so that when the final document has been reviewed we are in a good position to modify that accordingly.

PANEL MEMBER FUCALORO: Now these findings will be based upon what we have here, right?

PANEL MEMBER BLANC: Yeah, at the Chair's discretion.

CHAIRPERSON FROINES: Well, up to now what's happened is Stan has worked with Melanie to generate the first draft of the findings. And as far as I'm concerned I think that the next draft of the findings should come from Stan and Melanie.

PANEL MEMBER GLANTZ: Yeah.

CHAIRPERSON FROINES: And then I'll take it and review it before --

PANEL MEMBER GLANTZ: There was just a screwup, because these should have been circulated to the Panel in advance and I thought Melanie was sending them around and she thought I was sending them around.

PANEL MEMBER BLANC: Well, Stan, if you're going to be taking the lead on it, let me just point out a few things then.

PANEL MEMBER GLANTZ: Okay, well, you can do it afterwards, unless you want it on the record.

PANEL MEMBER BLANC: I think I'd like it on the

record. This won't take along.

As you've, yourself, alluded I'd like to see a parallel comment to the comment on ETS in terms of pesticides. You've already mentioned that yourself. And I'd like you in the Tier 2 compounds to highlight the ones that the sense of the Panel was that there was the most concern for.

And I'd like the polycyclic aromatic hydrocarbon findings to be less weighted towards carcinogenicity and to include the noncarcinogenic effects that were discussed, which had to do with, in particular, that there be specific discussion of naphthalene in the polycyclic.

So I'm just reiterating things that were --

PANEL MEMBER GLANTZ: Okay. I think that's all fine.

PANEL MEMBER BLANC: And I think that also what would be useful would be to follow the same advice for the findings as we suggested that they have that it comment on these two axes in terms of the evidence.

PANEL MEMBER GLANTZ: Differential. I see, differential and exposure.

PANEL MEMBER BLANC: Right.

PANEL MEMBER GLANTZ: That's all fine.

PANEL MEMBER FUCALORO: Because all that's in the record now, so I think that makes it very simple.

PANEL MEMBER GLANTZ: We don't have a quorum anymore or we could adjourn.

PANEL MEMBER BLANC: He's just gone out for a second.

So can I clarify then the timeline? The timeline will be that the final -- there'll be a final face-to-face public meeting to comment on the public comments or to address the public comments, is that the intention?

MS. HECK: That's the idea.

SUPERVISING TOXICOLOGIST MARTY: Hopefully by the end of July.

CHAIRPERSON FROINES: I'm sorry.

PANEL MEMBER BLANC: I was just clarifying that there is going to be a follow-up face-to-face meeting in which OEHHA will be commenting on the public comments and we'll be responding to OEHHA's comments on the public comments.

SUPERVISING TOXICOLOGIST MARTY: You will have had written responses.

CHAIRPERSON FROINES: And I'm hoping that that can occur in July, towards the end of July. But does that work, Colleen, in terms of the public having enough time to comment?

MS. HECK: We think, given how many iterations there have been and the fact that the stuff can be readily

gotten out there fairly quickly that it's about three weeks time that that should be adequate.

PANEL MEMBER GLANTZ: You mean from today?

MS. HECK: We're envisioning, yeah, that the close of the comment period would be in approximately three weeks.

CHAIRPERSON FROINES: So the public has the documents that we have, so if we go until something like July 15th that will be at least three to four weeks of --

PANEL MEMBER GLANTZ: Well, I think she had said July 6th.

MS. HECK: We were thinking July 6th, because we need to do responses and get them to you and to prepare for the meeting.

PANEL MEMBER BLANC: They'd end the public comment period July 6th and then we would meet two weeks later.

MS. HECK: Right.

PANEL MEMBER BLANC: There has to be a period for OEHHA to respond to the public.

MS. HECK: Right, otherwise there would be no time to do the responses and circulate them to the Panel.

PANEL MEMBER GLANTZ: Yes, but I think if they can do it, then we should.

CHAIRPERSON FROINES: I think this is awfully important and I'd like to make sure the public has sufficient time to comment. So if there could be a few days

more I wouldn't -- and I think it would be in our best interest.

SUPERVISING TOXICOLOGIST MARTY: That's fine, I think so too.

Let's make the Panel Meeting really the last part of July, instead of just kind of the last part of July.

PANEL MEMBER GLANTZ: Like the 18th or something?

MS. HECK: Closer to the 31st.

SUPERVISING TOXICOLOGIST MARTY: 29th, 30th, 31st. I don't have a calendar, so I don't know what days those are in the week.

PANEL MEMBER GLANTZ: All right. Well, do we have any other business?

CHAIRPERSON FROINES: No, I think -- I hope you agree that having the discussion on administrative matters would be best if everybody were here?

PANEL MEMBER GLANTZ: Uh-huh.

CHAIRPERSON FROINES: In which then there's nothing more for today. So we'll entertain a motion to close.

PANEL MEMBER GLANTZ: I so move.

PANEL MEMBER BLANC: Second.

CHAIRPERSON FROINES: All in favor?

(Ayes.)

CHAIRPERSON FROINES: We're done. Thank you.

(Thereupon the Air Resources Board Scientific Review Panel Meeting for June 15, 2001 was adjourned at 3:20 p.m.)

CERTIFICATE OF REPORTER

I, JAMES RAMONS, an Electronic Reporter, do hereby certify that I am a disinterested person herein; that I recorded the foregoing Air Resources Board Scientific Review Panel Meeting; that it was thereafter transcribed into typewriting.

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

IN WITNESS WHEREOF, I have hereunto set my hand this 25th day of June, 2001.

JAMES RAMOS

PETERS SHORTHAND REPORTING CORPORATION (916) 362-2345