

MEETING
STATE OF CALIFORNIA
AIR RESOURCES BOARD
SCIENTIFIC REVIEW PANEL ON TOXIC AIR CONTAMINANTS

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Dr. Gary Friedman

Dr. Stanton Glantz

Dr. Katharine Hammond

Dr. Joseph Landolph

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Dr. James F. Collins, Staff Toxicologist

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Dr. David Morry, Staff Toxicologist

Dr. Andy Salmon, Chief, Air Toxicology and Risk Assessment
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REPRESENTING THE DEPARTMENT OF PESTICIDE REGULATION

Ms. Tobi L. Jones, Assistant Director

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1 PROCEEDINGS

2 CHAIRPERSON FROINES: So I will officially
3 convene the meeting of the Scientific Review Panel on
4 Toxic Air Contaminants for May 19, 2004.

5 And I'll note that all the members of the panel
6 are in attendance with the exception of Roger Atkinson,
7 who was not able to attend.

8 And so this is the first meeting of the panel in
9 11 months, and we have a very lengthy agenda. And so
10 we'll try to move along as efficiently as possible.

11 So, Melanie, do you want to begin on
12 formaldehyde.

13 SUPERVISING TOXICOLOGIST MARTY: Sure. The --

14 CHAIRPERSON FROINES: And let me just ask one
15 question.

16 It's my understanding that Stan will only be here
17 till noon; is that correct?

18 PANEL MEMBER GLANTZ: Eleven.

19 CHAIRPERSON FROINES: Eleven.

20 PANEL MEMBER GLANTZ: And then I'll -- if there's
21 a phone, I can call in about 1:30.

22 PANEL MEMBER FRIEDMAN: I have to leave at noon.

23 CHAIRPERSON FROINES: Gary has to leave at noon
24 and Stan has to leave at 11.

25 That leaves 1, 2, 3, 4, 5 of us. So it's still

1 a quorum. But it's a significantly depleted panel, so
2 that --

3 PANEL MEMBER GLANTZ: They were -- the staff was
4 trying to arrange a thing where I could call in on the
5 phone. And I could call in about 1:30 till 3 to hear
6 the -- you know, to hear the afternoon stuff.

7 CHAIRPERSON FROINES: Okay.

8 PANEL MEMBER GLANTZ: The other thing is the part
9 of the agenda that I think I have the most to offer on is
10 the silica part. So you might want to take that into
11 account.

12 CHAIRPERSON FROINES: Well, the silica will come
13 up after formaldehyde. So we should be able to make that,
14 I hope.

15 PANEL MEMBER GLANTZ: I might be able to stay --

16 CHAIRPERSON FROINES: I don't know how long
17 Melanie and staff are going to present on formaldehyde.

18 So, anyway, everybody turn off your cell phones
19 if any have them on, so we don't have the noise.

20 So, Melanie, formaldehyde.

21 SUPERVISING TOXICOLOGIST MARTY: Okay. The first
22 agenda item is to discuss the formaldehyde petition.

23 (Thereupon an overhead presentation was
24 Presented as follows.)

25 SUPERVISING TOXICOLOGIST MARTY: The Formaldehyde

1 Epidemiology, Toxicology, and Environmental Group, now
2 called the Formaldehyde Council, petitioned the Air
3 Resources Board to reopen the risk assessment for
4 formaldehyde that was done under the Toxic Air Contaminant
5 Program back in the -- until early nineties. The petition
6 came to us in April 2002 with a number of appended reports
7 for OEHHA to consider.

8 OEHHA reviewed the material in the submission and
9 provided a response back to the Air Resources Board in
10 November 2002. We reviewed the petition with the petition
11 process in mind, which has specific criteria set out by
12 this panel back in '89.

13 Andy will present to you what our recommendation
14 was based on just the original submission using the
15 criteria in the SRP process. He will also present a
16 comparison of our cancer potency calculations with that
17 from the petitioner, and a brief summation of newer
18 epidemiology findings on potential links between leukemia
19 and formaldehyde exposure in industrial cohorts and
20 compare that to earlier findings on leukemia from earlier
21 epidemiology studies. That latter part is if the panel is
22 interested in that material.

23 Okay. With that I'm going to turn it over to
24 Andy.

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: Okay. Thank you.

2 Well, I'll try and work through this as
3 expeditiously as possible. So this is a presentation of
4 the petition materials and our response.

5 --o0o--

6 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

7 SALMON: The petition made a specific request of OEHHA and
8 the SRP that the 1992 risk assessment for formaldehyde be
9 reassessed because of the appearance of what they
10 described as new evidence, and requested review of this
11 new evidence. The main item in this new evidence is a
12 cancer risk assessment model which was laid out in a
13 report produced by CIIT in 1999. And the petition claims
14 that if this new evidence were accepted, it would change
15 the cancer potency value and possibly the identification
16 of formaldehyde as a carcinogen under environmental
17 exposure conditions.

18 --o0o--

19 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

20 SALMON: The materials included in the petition included
21 the CIIT report, various published papers -- included
22 various published papers and government reports and also a
23 PowerPoint presentation which was put together by the
24 petitioners on the -- which it went through the
25 development of the risk assessment presented by CIIT.

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1 --o0o--

2 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

3 SALMON: In addition to those materials which were
4 submitted with the petition, we received several other
5 items after the petition was received but before OEHHA
6 provided their response, including a copy of a report by
7 the NAK Committee of the German government and various
8 personal communications with Dr. Rory Conolly, who's the
9 lead scientist with CIIT on development of their risk
10 assessment. He was kind enough to assist us in
11 understanding the materials that had been presented and to
12 provide supplemental information that was necessary to
13 interpret that. And he also in fact gave a slide
14 presentation to ARB and OEHHA.

15 --o0o--

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

17 SALMON: In order to evaluate this petition, we basically
18 turned to the SRP's criteria for considering reevaluation
19 petitions and went through the various items.

20 The first item is: If the new evidence is
21 accepted, what's changed and how has it changed? We
22 examined the materials to see whether this would change
23 the determination of health effects, the determination of
24 threshold, all the derivation of a dose response
25 characteristics, which in this case would be in the

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1 carcinogenic potency.

2 The second requirement of a petition is that it
3 describe the importance of the new evidence as it relates
4 to the basis of the original risk assessment.

5 And the third criterion is that the petition
6 should demonstrate peer review of the new evidence.

7 --o0o--

8 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

9 SALMON: The OEHHA 1992 risk assessment identified
10 formaldehyde as a carcinogen with a potential to impact
11 humans. It found no evidence of a threshold. And it
12 presented a calculated cancer potency value of seven times
13 ten to the minus three per parts per million.

14 --o0o--

15 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

16 SALMON: OEHHA recommended denial of the petition on
17 evaluating it against these criteria on case 1a: The
18 evidence submitted with the petition does not change the
19 determination that formaldehyde is a carcinogen.

20 The qualitative evidence presented did not
21 include any new epidemiological studies or bioassays.
22 There is in fact in the literature that we already knew
23 about one updated bioassay which is in effect a repeat of
24 an existing one with additional dose levels. But that in
25 fact reinforces the original conclusion. So that doesn't

1 The petition argues that the CIIT report provides
2 evidence for a change of potency. However, this is
3 basically a reanalysis of existing data. And according to
4 the terms that we see, that doesn't necessarily constitute
5 new evidence.

6 And in terms of the analysis presented by CIIT,
7 unlike the assertion in the proliferation which describes
8 the OEHHA risk assessment as a default assessment, this is
9 not in fact the case. The OEHHA '92 risk assessment did
10 consider cell proliferation models and tissue-specific
11 deposition models in that earlier risk assessment.

12 --oOo--

13 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

14 SALMON: On grounds 1c, continued also, the material
15 submitted with the petition was not adequate to fully
16 evaluate the CIIT model. Although I mentioned earlier,
17 CIIT have been helpful in presenting us with additional
18 materials and information to help us evaluate that model.

19 But even with this additional materials, we
20 remain concerned that model uncertainty and uncertainty in
21 parameter estimates and uncertainty on the relative role
22 of mutagenic and proliferative responses, we are concerned
23 that these are inadequately addressed in the CIIT report,
24 and present a considerable level of uncertainty in their
25 final risk estimate.

1 --o0o--

2 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

3 SALMON: On criterion 2, the relationship to the previous
4 risk assessment, the petition failed to demonstrate
5 details of how the new model would change the OEHHA risk
6 assessment. And in fact, as I had mentioned earlier, it
7 incorrectly describes the OEHHA assessment as a default
8 method.

9 --o0o--

10 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

11 SALMON: We also had concerns under heading 3 relating to
12 peer review. Many of the critical calculations in the
13 CIIT report have not been peer reviewed by publication or
14 consideration by authoritative bodies. There were some
15 materials which had been published at the time of the
16 petition, but a considerable amount had not.

17 Since the petition was submitted, some new
18 material has been published. But this is still not a
19 complete peer review of the materials in the CIIT report.
20 And, in fact, the material published in some respects is
21 not exactly the same as what's presented in the CIIT
22 report.

23 --o0o--

24 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

25 SALMON: I'm now going to briefly compare the two risk

1 assessments, the OEHHA '92 and the CIIT '99.

2 --o0o--

3 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

4 SALMON: The OEHHA risk assessment is based on the 1983
5 Kerns rat bioassay. It presented a preferred estimate
6 of the -- of the unit risk as the upper confidence limit
7 for lifetime risk as seven times ten to the minus three
8 per parts per million. This used molecular dosimetry
9 data, which was based on some experimental measurements of
10 DNA protein cross-links, which you may find in subsequent
11 slides abbreviated as DPX.

12 The OEHHA risk assessment considered both
13 linearized multi-stage models and cell proliferation-based
14 clonal growth models. And it also considered scaling
15 factors based on either surface area considerations,
16 breathing rate, and absorption ratio. And it also
17 considered the impact based on either a systemic or
18 point-of-application basis.

19 So there are several different bases considered
20 in the risk assessment for all of these aspects of the
21 calculation.

22 --o0o--

23 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

24 SALMON: This is shown diagrammatically in this model. We
25 considered either an applied-dose or a tissue-dose model.

1 We considered linearized multi-stage model and cell
2 proliferation models. We considered various bases for the
3 scaling factor.

4 --o0o--

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

6 SALMON: And, in fact, as you see in this table, we
7 produced a range of estimates. And the one which was
8 presented as the best estimate is within this range. It's
9 somewhere in the middle of the range. It's actually a
10 three-stage multi-stage model using a scaling factor which
11 assumes systemic impact. And it uses the tissue-dose
12 calculation based on DNA protein cross-links. And so this
13 was the selected value from that range.

14 And this in fact compares with the EPA 1987 value
15 of 15 times ten to the minus three per parts per million,
16 which is within the range of estimates which OEHHA
17 produced, although it's about twice the preferred value
18 that was selected. The EPA model, in fact it is something
19 of a default model. So OEHHA went beyond that approach in
20 producing the estimate.

21 --o0o--

22 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

23 SALMON: The CIIT model uses -- risk assessment uses a
24 complex computational fluid dynamics model to assess the
25 area and extent of deposition of formaldehyde in the

1 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

2 SALMON: This is -- the next two slides I'm going to
3 compare the actual predicted dose response between these
4 two models.

5 This first slide shows two curves from the OEHHA
6 risk assessment. The upper curve, which is fairly linear
7 in this range, in fact is the default model, which is
8 rather similar to the one used by U.S. EPA. That upper
9 curve is applied-dose model. Whereas the lower curve,
10 which is, you can see, is somewhat -- somewhat nonlinear,
11 in fact is the OEHHA value -- that's the one which the
12 OEHHA preferred value is based. And that does use the
13 tissue-dose calculation based on DNA protein cross-links.

14 So you can see that applying that model feature
15 does have a significant effect on the overall risk
16 prediction.

17 --o0o--

18 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

19 SALMON: This -- I hope you can see the yellow curve on
20 this. This is basically data from CIIT. It may show up a
21 little better on the printed versions that you have. Or
22 is it equally bad there? I'm sorry.

23 Is there any -- well, I don't know whether we can
24 get the lights down at all.

25 I had hoped we would have a pointer, but we don't

1 seem to have a pointer here.

2 SUPERVISING TOXICOLOGIST MARTY: Thank you, Stan.

3 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

4 SALMON: Anyway, the distinctive feature of this dose
5 response is that there's a very strong point of inflection
6 somewhere in the range around .5 to .7 parts per million.
7 Theoretically the risk prediction rises very rapidly for
8 levels above that range. And CIIT characterized that
9 range as important for occupational exposures. But they
10 claim that the lower risk range, which is in fact in this
11 graph presented with the purple dots, is characteristic of
12 environmental exposures, and the slope is much lower.

13 --o0o--

14 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

15 SALMON: An important point to note about this is shown in
16 the next slide. This is the same environmental points as
17 were in the previous slide, but with a different scale.
18 And the important point to note is here, is that even with
19 this model, the -- there is in fact a predicted dose
20 response relationship. It's just less -- it's
21 considerably lower. And we had some points to make about
22 that.

23 But that's the -- the critical difference in the
24 two predictions is that the CIIT model predicts a very,
25 very strong point of inflection.

1 --o0o--

2 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

3 SALMON: From exposure at .1 parts per million, which
4 would be in the environmental range, the CIIT estimate's
5 in fact four orders of magnitude lower than the risk
6 prediction from the OEHHA model.

7 --o0o--

8 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

9 SALMON: The reason that they are so different is
10 basically that the interaction of their fluid dynamic
11 model, which predicts a highly nonlinear relationship
12 between the applied dose and the deposition in various
13 areas of the respiratory tract, so that much of the impact
14 is in a few small areas of the respiratory tract in the
15 lung. Whereas they're not predicting such a strong
16 concentration in the human respiratory tract.

17 PANEL MEMBER FRIEDMAN: Could I interrupt?

18 What's DPX stand for?

19 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

20 SALMON: DNA protein cross-links.

21 So that the use of this fluid dynamic model and
22 the way it interacts with the subsequent stages of the
23 cell proliferation model is one reason why there would be
24 a considerable difference. And in this case OEHHA used
25 empirical DNA protein cross-link data, whereas CIIT

1 considered the DNA protein cross-link formation to be
2 following this highly nonlinear and highly
3 geographically-specific model which they developed.

4 --o0o--

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

6 SALMON: Because of this deposition model which they used,
7 the inputs to the two-stage cell proliferation model are
8 nonlinear. So you basically have two interacting
9 nonlinear models here. And the effect of this is that
10 very small changes in the input values can make big
11 differences in the risk prediction. And so those inputs
12 can change both the slopes of the different phases of the
13 dose-response curve, which you saw in the earlier slide
14 which I presented which you couldn't read, and they can
15 also make changes in the position of the point of
16 inflection. So both of those features of that
17 dose-response curve we regard as being highly uncertain
18 because they're susceptible to changes in the parameter
19 inputs for these highly nonlinear models.

20 --o0o--

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: I'm going stop here for a moment. And Melanie
23 will --

24 SUPERVISING TOXICOLOGIST MARTY: Dr. Froines, I'm
25 just wondering if you want to stop here and talk about the

1 information that was submitted to OEHHA in the petition,
2 or if you want us to make a few comments on the new
3 epidemiological studies which have been published since
4 the petition was submitted.

5 CHAIRPERSON FROINES: Well, let me ask Gary about
6 that.

7 Gary, do you -- would you like them to --

8 PANEL MEMBER FRIEDMAN: Yeah, I'd like to have
9 them present that.

10 CHAIRPERSON FROINES: Go ahead.

11 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

12 SALMON: I'll continue then.

13 --o0o--

14 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

15 SALMON: One of the things which we've become aware of in
16 fact since we considered the OEHHA recommendation to the
17 panel about the petition is that there have been three
18 important new epidemiological studies which have been
19 published. These are shown here. And these include
20 findings that might impact the basis and conclusions of a
21 revised formaldehyde risk assessment.

22 --o0o--

23 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

24 SALMON: Basically what these studies are, they are
25 updates of existing cohorts which have previous -- about

1 SALMON: It varies somewhat according to the studies. But
2 it's usually some -- some combination of different values.
3 In fact, sir, the recent papers do include consideration
4 of several alternative measures of exposure. This is, if
5 you like, the simplest and crudest overall value plotted
6 here.

7 But I think what you can see is that, although
8 none of the individual findings are actually clearly
9 significant, and although one or two of the studies
10 actually don't find an association, nevertheless there's a
11 kind of weight of findings over on the side of there being
12 some kind of an association.

13 So -- yeah, these are -- the axis here is just an
14 ordinal scale. These values are ordered in terms of the
15 increasing average or mean value for the risk ratio.

16 PANEL MEMBER FRIEDMAN: Can I interrupt there for
17 a second.

18 Normally -- I mean it's preferable to express
19 relative risk on a log scale, in which case the lower
20 parts -- the studies that show a risk below 1.0 would be
21 stretched out and might not give the same impression of
22 the weighting that you described as being --

23 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

24 SALMON: Yes, I accept that. I fear this was put together
25 in a little bit of a hurry. So if and when we come to

1 evaluate this in more detail, we'll obviously take your
2 advice into account and make any such prediction. This is
3 merely an attempt to say this is out there at this point.
4 We don't pretend that we've been able to do an analysis of
5 this.

6 PANEL MEMBER FRIEDMAN: It does show that those
7 new findings fit into the --

8 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
9 SALMON: Yes. That I think is the point, that the new
10 findings are consistent with the earlier findings, which
11 were analyzed to some degree in the '92 report. So we're
12 not talking about anything which is radically new here.
13 But the new studies are larger, they use more up-to-date
14 methodology.

15 --o0o--

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
17 SALMON: And although the overall results are not so
18 convincing, if you look at their more detailed analysis,
19 both the Hauptmann and the Pinkerton study present a
20 sub-cohort analyses, which include some values which
21 actually are statistically significant. And the elements
22 of selection which point to those statistically
23 significant sub-cohorts basically include specifically
24 myeloid forms of leukemia, either acute or chronic, as
25 opposed to all the leukemias. So there's a biological

1 sensitivity analysis on the CIIT model? I mean you said
2 that it was highly nonlinear. But did you do any kind of
3 quantitative analysis to see how varying the assumptions
4 within a reasonable range would affect how their
5 predictions compared to what you guys had done before?

6 STAFF TOXICOLOGIST MORRY: This is David Morry,
7 OEHHA.

8 What I did is I got some parameters from Dr. Rory
9 Conolly. And I attempted to reproduce the cell
10 proliferation model -- part of their model, not the
11 computational fluid dynamics part.

12 What I found is -- and I ended up with similar
13 result to theirs using their -- the parameters they sent
14 me.

15 What I found is if you -- there are two inputs to
16 that model. One is the mutation rates for the changes of
17 one cell type to another. And the other input is the rate
18 of proliferation of the cells. What I found is that the
19 model is far more sensitive to the rate of proliferation
20 of the cells parameters than it is to the mutational
21 parameters. So if you vary the parameters that had to do
22 with cell proliferation only a little -- only a tiny
23 amount, you get a huge difference in the cancer risk
24 prediction that comes out of the model.

25 PANEL MEMBER GLANTZ: And what do you mean by

1 huge?

2 STAFF TOXICOLOGIST MORRY: Well, you can tweak it
3 a little bit and it will just go astronomical in one
4 direction or another.

5 PANEL MEMBER GLANTZ: But I mean how much would
6 you --

7 STAFF TOXICOLOGIST MORRY: I did not do a
8 quantitative sensitivity analysis of the model.

9 PANEL MEMBER GLANTZ: I mean I think an important
10 question would be, you know, if it is that sensitive --
11 and those sorts of nonlinear models can be -- you know,
12 how much would you have to change the input parameters to
13 end up with risk results that were comparable to what
14 OEHHA had come up with based on the earlier -- you know,
15 the earlier analysis?

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
17 SALMON: Well, obviously --

18 PANEL MEMBER GLANTZ: Does that make sense as a
19 question?

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
21 SALMON: Obviously that's doable because that's in fact
22 what OEHHA did in '92, is that they ran a cell
23 proliferation model using a different but still plausible
24 selection of parameters and came up with risk predictions
25 which were similar to, and in some cases higher and some

1 cases lower, but definitely within the range of the value
2 that was selected eventually as the best value in '92.

3 PANEL MEMBER GLANTZ: But, see, the point I'm
4 making here is it may be that there isn't -- if the model
5 is indeed as sensitive as you're suggesting, it may be
6 that there's not a difference -- you know, a big
7 difference in terms of the estimated risks within
8 reasonable parameter sets, which I think would be worth
9 checking.

10 STAFF TOXICOLOGIST MORRY: If formaldehyde has a
11 much -- has a smaller effect on cell proliferation than
12 the one estimated, then the risk could be very much lower
13 or very much higher. So by tweaking that parameter, the
14 cell proliferation parameter, you can change the risk
15 estimate by orders of magnitude. So changing the cell
16 proliferation parameter in the right direction would make
17 the CIIT model produce the same numbers that the OEHHA
18 found --

19 PANEL MEMBER GLANTZ: Right. But the question
20 is -- I mean it's true -- I mean if you just -- I'm sure
21 you can pick some number that will make it do that. But
22 the question is: If you pick values that are reasonable
23 based on what we know about the biology, would that
24 happen?

25 STAFF TOXICOLOGIST MORRY: I think that can be

1 done with, you know, biologically plausible cell
2 proliferation rates.

3 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
4 SALMON: It's important to note that the CIIT model
5 actually uses parameter values which are optimized in
6 order to fit the bioassay data. So in a sense they're not
7 using, quote-unquote, "independently determined biological
8 parameter values". They're using values which, you know,
9 fit the data the way they like the data to be fit.

10 And so, you know, the short answer is that
11 there's probably several ways that you could do that
12 depending on which -- you know, which angle you chose to
13 look at the data from.

14 SUPERVISING TOXICOLOGIST MARTY: I'd just like to
15 add one other issue to that. And, that is, that under SB
16 25 in California we're supposed to be considering
17 children. And the cell proliferation rates would very
18 likely vary by age. And there is no information on that
19 in the CIIT model. And that would also impact whether the
20 potency varies by age under their model.

21 PANEL MEMBER FRIEDMAN: Which way would it go? I
22 mean if the cell proliferation rate was higher in
23 children, would that make the potency higher?

24 SUPERVISING TOXICOLOGIST MARTY: Yes, it would.

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: It would also possibly change the -- not only the
2 slope of the curve in the different sections, but also
3 possibly change the point -- the position of the point of
4 inflection, which is potentially important because it's
5 very close to the sort of division between the
6 occupational levels and levels which are certainly
7 plausible as being in the higher end of environmental
8 range. And it could also change the relationship between,
9 you know, the degree of -- the degree of difference
10 between the low dose and high dose slopes.

11 CHAIRPERSON FROINES: Are there further questions
12 before we return to the leads for this issue?

13 Stan, are you satisfied with where you are?

14 Okay. The three leads on this issue are Gary
15 Friedman, Joe Landolph, and myself.

16 And so why don't we turn first to Gary and then
17 go to Joe.

18 PANEL MEMBER FRIEDMAN: John asked me to look at
19 the three new epidemiologic --

20 CHAIRPERSON FROINES: I don't think you're close
21 enough.

22 PANEL MEMBER FRIEDMAN: John asked me to look at
23 the -- is that working? -- to look at the three new
24 epidemiologic studies that were just presented here, and
25 to see if I thought that that would indicate the need for

1 a new risk assessment by OEHHA.

2 And the original risk assessment acknowledged
3 that the epidemiologic data were inconclusive and the risk
4 assessment was based on, as we feared, extrapolation from
5 animal models. And I think the situation was not
6 changed -- has not been changed by these three new
7 studies. They're also inconclusive in terms of whether
8 you can judge that there's a causal relationship between
9 formaldehyde exposure and leukemia or lung cancer or the
10 others that were looked at in these papers.

11 So I think the situation remains the same, and I
12 don't think the new epidemiologic evidence is sufficient
13 reason to conduct a new risk assessment.

14 CHAIRPERSON FROINES: Questions for Gary?

15 The degree of succinctness is overwhelming.

16 Joe.

17 So -- well, just before we go to Joe, Andy, do
18 you want to comment on what Dr. Friedman said, or David or
19 Melanie?

20 SUPERVISING TOXICOLOGIST MARTY: Well, I hate to
21 argue with an epidemiologist since I'm not one. But the
22 one thing that struck us was that the -- particularly the
23 Hauptmann studies appeared to be a pretty well conducted
24 study. We had a number of folks at OEHHA who are
25 epidemiologists read it. Of course this was, you know,

1 without the context of all the other information that
2 these folks were reading it. But we were struck by the
3 demonstration in our mind of dose response in the
4 Hauptmann study, that they went to a great deal of effort
5 to characterize exposure. Although, unfortunately, it's
6 not described in that paper; it's described elsewhere. So
7 we thought it kicked it up a notch.

8 CHAIRPERSON FROINES: Well let me ask you a
9 question, going on his conclusion.

10 If you were to redo the risk assessment at this
11 point, would you use the Hauptmann study as the basis for
12 your risk determination or would you continue to use
13 animal data? In other words, do you have sufficient
14 confidence in the Hauptmann study that you would
15 actually -- do you think that you would actually alter the
16 basic information you use for the risk assessment?

17 SUPERVISING TOXICOLOGIST MARTY: I think -- we
18 would certainly look at it closely in conjunction with all
19 the other information on any potential link between
20 formaldehyde exposure and leukemia, and we could make
21 estimates based on that. Whether it would be -- we would
22 also look at all of the animal data. And, you know,
23 whether the epidemiology would be the basis for the number
24 we chose, I really can't say right now because we actually
25 haven't done that analysis. But we'd certainly look at

1 it.

2 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

3 SALMON: I think the point is that we wouldn't have the
4 data on which to base that choice until we did the
5 reassess -- the risk assessment. But what I suspect would
6 happen if we -- you know, if for whatever reason the panel
7 were to direct us to do a formaldehyde risk assessment
8 reevaluation, there is no doubt that we would look at
9 these epidemiological data and attempt to produce some
10 kind of probably highly uncertain risk estimate from them,
11 and that we would at least be -- we would need to do
12 something similar to what we've done in a number of other
13 risk assessments, is to calculate a human value as best we
14 can and see whether or not that's consistent with the
15 animal data.

16 And if it is, then we might take that into
17 account in predicting an overall risk value. But as to
18 how much weight we would put on the human data versus the
19 animal data, I don't think we can -- we can't answer that
20 until we've done the assessment, which clearly we've not
21 at this point.

22 CHAIRPERSON FROINES: Gary.

23 PANEL MEMBER FRIEDMAN: Well, I want to agree
24 with Melanie, that I thought the Hauptmann study was very
25 well done and impressively conducted and, you know, is

1 really a thorough discussion of limitations and strengths
2 and so on. I think there were some inconsistencies in it.
3 There was an association with the average and peak
4 exposure levels but not with accumulative exposure. So
5 there are some questions that were difficult to answer.

6 And I wanted to ask, in that nice slide that you
7 showed, which I comment about the use of log scale, but
8 still you did line up all the studies of leukemia, has
9 there been a meta-analysis to show what the overall risk
10 is based on all of these data?

11 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

12 SALMON: There has been one put together by the -- I think
13 by -- is it Dow Chemical? -- yeah, by an analyst from Dow
14 Chemical. I'm not sure that what we have -- I'm not sure
15 what we have at this point is, you know, a comprehensive
16 academically validated meta-analysis. This is something
17 which would need to be looked into.

18 PANEL MEMBER FRIEDMAN: I think it might be a
19 worthwhile effort.

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

21 SALMON: Yes. I would certainly think that such an
22 analysis would be required in order to consider the human
23 data properly. And, as I say, I think if we were to be
24 instructed to do a reevaluation, then that's clearly
25 something that would have to be included in that

1 evaluation.

2 CHAIRPERSON FROINES: Yeah. I'm asking my
3 questions basically not to create a difference between
4 what Gary said, which I agree with, and OEHHA. I'm trying
5 to get -- I was simply trying to get at the issue of,
6 within the context of epidemiology, when is something
7 sufficiently demonstrated that one feels confident that it
8 would be appropriate to use for purposes of risk
9 assessment?

10 And what I hear -- the question on meta-analysis
11 an interesting one because, depending upon the results,
12 one might argue that perhaps it is ready. But it's still
13 sort of in -- it seems like it's in a gray zone. And one
14 would like to see some more confirmatory data before one
15 did that. But, again, maybe it's closer than -- maybe
16 it's closer than I think anyway.

17 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
18 SALMON: For what it's worth, the Dow Chemical
19 meta-analysis did not -- you know, it did not confirm
20 the -- or they didn't regard it as showing evidence of a
21 strong association that could be considered causal.

22 PANEL MEMBER FRIEDMAN: Did that include the
23 Hauptmann study?

24 SUPERVISING TOXICOLOGIST MARTY: Yes, I think so.

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: I believe it did. But I don't know on what
2 basis. I don't have the details of that.

3 CHAIRPERSON FROINES: Kathi.

4 PANEL MEMBER HAMMOND: It seems to me that in
5 the -- you presented a one-point estimate and -- and
6 constant set of limits of the entire data. But when you
7 break it down by the exposure groups, that's where the
8 dose response appears.

9 And also I was struck at the large -- the largest
10 exposure group in the analysis in Hauptmann were
11 statistically significant. And obviously those are
12 smaller numbers. So, you know, the point estimate is
13 higher. And that that's actually consistent with the
14 Pinkerton paper as well.

15 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

16 SALMON: Yes.

17 PANEL MEMBER HAMMOND: But that was -- you know,
18 so as it looked on the graph as you had it, it looked like
19 they were not statistically significant and they all went
20 under one. But I think when you look at the actual values
21 and you stratify it by exposure levels.

22 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

23 SALMON: Yes. The overall analyses are not statistically
24 significant. But there are several as a subgroup
25 analysis, including the dose response thing --

1 PANEL MEMBER HAMMOND: Right. I think that's
2 particularly important.

3 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

4 SALMON: Yes. Well, I think it has to be said that, you
5 know, one of the reasons why people would probably think
6 these papers strengthen the plausibility of the
7 association is because of two things: There's the things
8 like the dose response observed in Hauptmann and the time
9 dose responses observed by Pinkerton. And the other thing
10 is the indication of, you know, an apparent biological
11 selectivity for the myeloid type of leukemia.

12 Now, this is obviously saying that -- you know,
13 this evidence has more weight than what we had before.
14 The question is, does it have enough, you know, to form --
15 and I think we're clearly at this point -- you know, we
16 defer to Dr. Friedman's opinion on that, because he's the
17 panel's expert. But, yeah, there's no doubt that the new
18 data are more convincing than what we had before and would
19 need to be considered were we to be instructed to do a
20 reevaluation.

21 CHAIRPERSON FROINES: Gary.

22 PANEL MEMBER FRIEDMAN: I think the other
23 question that, you know, is a big one in relation to
24 formaldehyde exposure in leukemia is the one of biological
25 plausibility. And there was discussion in the papers as

1 to whether formaldehyde can get far enough beyond the
2 mucous membranes to get into the bone marrow and affect
3 stem cells, and so on, and induce them to change into
4 leukemic cells.

5 But we received some references, I think thanks
6 to Eleanor, showing that there were stem cells in the
7 circulating blood and that -- so if they're going from
8 capillaries near the surface of the -- say, the nasal
9 mucosa, they could be exposed to formaldehyde. So that I
10 think that it is a biologic -- it is biologically
11 plausible that that could induce leukemia.

12 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

13 SALMON: There are also data showing appearance of
14 chromosome aberrations, micronuclei cystochromes in
15 exchanges in humans exposed to formaldehyde vapor.

16 So -- I mean another purely philosophical point
17 of view is if you were in a position where you felt the
18 epidemiological data were convincing, then, you know,
19 plausible or not, you'd have to get used to it. And it
20 would be up to the mechanistic analysts to explain an
21 observation. I suppose while things are uncertain, then,
22 you know, there's room for debate about plausibility,
23 but --

24 CHAIRPERSON FROINES: We sent the references that
25 Gary's referring to to the panel. And I've just -- but I

1 know that some people -- Kathi and Stan have been
2 traveling, so they may not have it. So we'll get Peter --

3 PANEL MEMBER GLANTZ: What are those?

4 CHAIRPERSON FROINES: These are the references
5 that relate to the issue of biological plausibility.

6 So if everybody's comfortable.

7 But I think, Peter, we should still have them for
8 people in the audience. These are --

9 PANEL MEMBER GLANTZ: That was the thing -- that
10 was the list of -- was that the list of references of
11 first a list of characterization of -- yeah, I got those
12 last week, I think.

13 CHAIRPERSON FROINES: Are those back there?

14 MR. MATTHEWS: No.

15 CHAIRPERSON FROINES: They should be. I think
16 that --

17 PANEL MEMBER GLANTZ: Aren't there some other
18 leads we haven't heard from?

19 CHAIRPERSON FROINES: Yeah, absolutely. But I
20 just wanted to make one comment before going forward.

21 I think that the people misunderstand the term
22 "limited" in the IARC evaluations. And it's one of these
23 issues of the glass is half full or the glass is half
24 empty. And I think it's important to emphasize that the
25 term "limited" in terms of epidemiologic studies is

1 generally perceived as a positive statement about the fact
2 that there is evidence of epidemiologic findings showing
3 positive results. It is -- limited does not -- should not
4 be taken as a negative statement. In fact, it's just the
5 opposite.

6 And so that one question -- there are two issues:
7 One has to do with the qualitative question of, is
8 formaldehyde a toxic air contaminant? Is there evidence
9 for its carcinogenicity? -- which is a "yes-no" question,
10 a qualitative question. And then there's the quantitative
11 issue of risk assessment.

12 And in your view would these studies -- may not
13 be useful yet at least with the level of analysis that
14 you've done to suggest that they should be used for risk
15 assessment purposes. But do they add to the weight of
16 evidence on the "yes-no" question of whether
17 formaldehyde's a carcinogen?

18 SUPERVISING TOXICOLOGIST MARTY: I think the
19 answer is yes, that they add to the weight of evidence
20 that formaldehyde is a carcinogen.

21 CHAIRPERSON FROINES: Okay. Joe.

22 PANEL MEMBER LANDOLPH: We received a truckload
23 of data on this one. I did read it all. And I was struck
24 by a number of things. Of course the rat model leading to
25 the concentration of formaldehyde in a nasal -- a specific

1 nasal area is interesting, and I had some questions as to
2 whether --

3 PANEL MEMBER FRIEDMAN: Excuse me. Could you
4 speak up a little louder.

5 PANEL MEMBER LANDOLPH: Sure. Sorry.

6 And I had some questions as to whether when you
7 spread that over the mouth and the nose in humans and
8 monkeys, maybe that would make the various
9 regional-specific areas show a lesser risk. So it may be
10 a little complication of going from a rat model to a
11 human.

12 I liked intellectually the model. I think the
13 model's intriguing. There's a lot of academic component
14 to it. But I'm not convinced myself that there is enough
15 new data, just on a data basis alone, to merit a
16 reconsideration.

17 I would recommend that OEHHA take a leadership
18 role in thinking about these models and determining
19 whether they think they're worthy for implementation in
20 the future, because I think this is a future science
21 starting to break over us and I don't think we can ignore
22 it forever.

23 Having said that, at the same time I still would
24 urge caution, because certainly the linear ice multistage
25 model is a conservative model; and I think before we

1 depart from that, there should be a very good reason for
2 it. I'm concerned that the Conolly report is very
3 intriguing intellectually, but I don't think it represents
4 a substantial amount of new data as far as I can
5 determine.

6 And I want to thank the presentation of Dr.
7 Salmon and Dr. Marty.

8 I had the same feeling about this model because
9 it's a very parameter-rich model as well as data rich.
10 But the parameter rich bothers me a little bit. And
11 particularly this being able to manipulate the cell
12 division rates and cell death rates, as Dr. Morry so
13 eloquently pointed out, can lead to large changes in the
14 estimated cancer risk. So I have a natural skepticism
15 about that, and I had it when I first looked at this
16 model.

17 So I think I would urge you to take a look at the
18 model and see whether in the future iterate a modified
19 version of it might be useful in modern risk assessments,
20 because I don't think we can ignore that new -- the new
21 conceptual science breaking.

22 I'm extremely bothered by the fact there's a four
23 order of magnitude difference between that model and the
24 prior models. And I don't think that that four order of
25 magnitude difference is based on the acquisition of new

1 data. I don't believe that. So that makes me even more
2 skeptical of the application of the model at present.

3 So I guess my position would be one where I would
4 say please look at the model, please look at the new
5 science as it develops. But based on data alone, I don't
6 think there's a necessity to do the reevaluation. If
7 OEHHA comes up with a hybrid model or a version of this
8 model which is reasonable and it's not so susceptible to
9 manipulation by a parameterization, then I would urge you
10 to begin thinking about applications of this in the
11 future. But I would still urge some conservatism in this
12 area to protect public health.

13 CHAIRPERSON FROINES: Okay. Questions for
14 Stan -- for Joe?

15 PANEL MEMBER GLANTZ: I'll take the questions.

16 (Laughter.)

17 PANEL MEMBER BYUS: How was the drive from San
18 Francisco to Oakland, Stan?

19 PANEL MEMBER GLANTZ: I got lost.

20 CHAIRPERSON FROINES: Okay. What I did was --
21 like Joe -- and Joe and I've had a number of conversations
22 about this issue. This is a very complex petition,
23 because you have dosimetry data that's been advanced, you
24 have new approaches to modeling that have been advanced,
25 there's new epidemiologic data. And so in my view, I

1 thought that the panel would benefit from expertise in the
2 area of risk assessment and toxicokinetic modeling. And I
3 knew that Dale Hattis in the early eighties, who is
4 without doubt one of the three or four leading risk
5 assessment experts in the United States -- and I think we
6 would all agree with that -- had worked on formaldehyde in
7 the early eighties.

8 So I contacted Dale and asked him to serve as a
9 consultant to the panel. And he agreed. And he has
10 written a report, which everybody on the panel here has,
11 and is -- I think there are copies in the back for those
12 that don't have it. And Dale was the person who actually
13 provided the references that we talked about earlier with
14 respect to Gary and the biological plausibility.

15 And I think that this, done in a relatively short
16 time, is an extremely useful and informative document for
17 us. And I think, however, that it has two implications.
18 And one implication is that Dale Hattis is our consultant
19 to this panel, so his findings have to have significant
20 weight for the panel, I think. And in that regard Dale
21 draws the following conclusions: And I'll read -- I won't
22 read the whole document, but I'll read the three
23 conclusions.

24 One is: "There are certainly elements of the
25 CIIT model that represent potentially helpful advances on

1 the prior state of the art."

2 So that he is saying in that sentence that the
3 CIIT model does represent new information.

4 PANEL MEMBER BLANC: No, I would disagree with
5 that interpretation. He's saying it represents a new
6 approach. It's not new information. I think that's a
7 very critical difference. It's not new original data.
8 It's a proposed hypothetical view of existing data. And I
9 think that's critical.

10 CHAIRPERSON FROINES: We should discuss that.
11 Because, yes, you're right. But the criteria don't limit
12 us to deciding that the data has to be new. One can take
13 a new approach, and one consider that a new advancement of
14 the science.

15 PANEL MEMBER BLANC: I think it's more than just
16 a semantic difference. So maybe we'll return to that.
17 But I think it has to do with the difference between
18 whether or not the OEHHA's scientific evaluation of the
19 petition is appropriate scientifically from the panel's
20 point of view, which is what we're being asked to comment
21 on, as disassociated from the question of: That being
22 said, how should the information that has arisen as a
23 result of reviewing the petition be potentially applied to
24 other activities that OEHHA can embark upon? For example,
25 the way it's going to have to deal with formaldehyde and

1 the childhood risk assessment and ways in which it may
2 more globally look at risk assessment models that involve
3 nasal absorption and so forth.

4 I think those are two separate things.

5 CHAIRPERSON FROINES: Let me finish.

6 He also goes on to say: "There is some new
7 science here. However, the analysis has not been carried
8 forward far enough to be able to make an apples-to-apples
9 comparison with the OEHHA/ARB upper confidence limit
10 estimate."

11 And he then goes on to say that: "There is at
12 least one additional helpful type of treatment of the
13 CIIT data, some of which are new, such as the additional
14 tumor findings reported here for the first time. This is
15 an integrated treatment of the two pathways of
16 carcinogenesis, reflecting both cell proliferation and
17 mutagenic effects. This can be done..." and so on and so
18 forth.

19 So I understand Paul's questions. But I think
20 that at some level Dale is saying, is concluding that
21 there is new information here. Whether that's
22 methodologic or actual scientific data I think is
23 something we need to discuss.

24 But having said that, the other conclusion that
25 one would draw from this is that he is highly critical of

1 the CIIT approach at the same time. And I'm not going to
2 go through and read that. Everybody can read it. And I
3 talked to him this morning. And he felt -- and this is my
4 notes from the phone conversation. He felt that, quote,
5 "it's critical that the model be evaluated for
6 uncertainties for the magnitude of the low dose linear
7 component and include interactions with background cell
8 replication rates and background mutation and stem cells
9 susceptible to carcinogenic transformation."

10 He has questions, as Stan's raised, about the
11 nonlinearity and the dose response relationship, but he
12 hasn't looked into that portion of the data. And he
13 thinks that that nonlinearity will go away if one develops
14 an upper confidence limit on what is -- what CIIT calls
15 their KMU, but it is in some respects similar to a Q start
16 in our normal terms.

17 And he says that "the data is at this point not
18 sufficient to arrive at a new upper bound risk analysis.
19 It is not sufficient for a new estimate of the upper bound
20 risks that could be associated with formaldehyde at
21 environmental and occupational levels."

22 So that what Hattis is saying, I think, is in a
23 sense two things: That there are new approaches, there is
24 new toxicokinetic modeling, there is new risk assessment
25 methodology, there's some new biological data on the one

1 hand; and on the other hand he's saying that there isn't
2 sufficient evidence to develop a new upper bound estimate
3 for the risk analysis. And so he's saying that based on
4 the materials that he reviewed for this petition, that
5 this information is not sufficient for estimation of the
6 ultimate risk.

7 And so he would argue I think based on the two --
8 my discussion with him and the document, that, whereas
9 there is new information -- and we can quarrel over the
10 differences in that respect -- but that the data -- but
11 that the methodology is not sufficient for evaluation at
12 this point. So that would be his conclusion.

13 PANEL MEMBER FRIEDMAN: Well, could I -- there
14 was something that you sent, I think it was a memo to the
15 committee, in which you made three points. And I think
16 one of the points you said was that there should be a new
17 evaluation. And I didn't get that from our phone
18 conversation. I think you said we may have this three-way
19 conversation of the three lead people. And that one of
20 the conclusions was, yes, there should be a new
21 evaluation. And I didn't come away from the conversation
22 remembering that.

23 CHAIRPERSON FROINES: Oh. Well, my view at this
24 point is that there are a number of -- there may be four
25 points that I would conclude.

1 The first and most significant point that I think
2 we need to conclude is that there is no evidence submitted
3 to date that would change our conclusion that formaldehyde
4 is a toxic air contaminant, that our view in 1992 is the
5 same as our view today. Formaldehyde is a toxic air
6 contaminant based on the information in the petition and
7 the new epidemiologic data and so on and so forth. So
8 there findings are consistent with that.

9 I think we should also say that the CIIT petition
10 does represent a new approach and does contain some new
11 information. And I would argue as a person who does work
12 in toxicokinetics that that would constitute relevant new
13 information from the standpoint of risk assessment.

14 And so I would argue that there is new
15 information. I would argue based on Hattis' review that
16 that information is not yet sufficient to define a new
17 risk assessment by OEHHA were OEHHA to take it up. So
18 that the data is not -- the analysis done by CIIT requires
19 extensive new work based on what Dr. Hattis -- what Dale
20 Hattis says.

21 Fourth, I would say -- one of the things that was
22 alluded to is that OEHHA is going to be looking at risk
23 assessment methodology as part of the SB 25 process. So
24 they're going to be looking at risk assessment
25 methodology. And they have to look at some tier 2

1 compounds, and formaldehyde is a tier 2 compound.

2 So I could foresee a process in which CIIT
3 developed their risk assessment model more fully, that
4 they submitted that to OEHHA, and that while OEHHA was
5 doing their tier 2 review following their risk assessment
6 methodologic evaluation, that they'd look at formaldehyde
7 within the context of the updated CIIT input --
8 formaldehyde industry input as part of their tier 2
9 process.

10 PANEL MEMBER FRIEDMAN: So we're not asking
11 them -- according to what you're recommending, we're not
12 asking them to do anything that they wouldn't ordinarily
13 do under the SB 25 process, is that --

14 CHAIRPERSON FROINES: Well, I think they should
15 respond and say that that would be appropriate if we took
16 that approach. Because I've just listed basically a
17 four-step approach. One is to acknowledge that there is
18 some information, but that it doesn't affect our TAC
19 determination; that there is more work to be done by CIIT
20 to deal with some of the issues that -- Stan actually
21 raised many of the same issues that in fact Dale did.

22 So I think it's not just Hattis' view. And that
23 CIIT would then submit subsequent risk analyses based on
24 what was requested; and that when OEHHA was dealing with
25 their tier 2 compounds and was looking at the risk

1 assessment of formaldehyde in the context of SB 25, that
2 they would then look at that new formaldehyde data from
3 CIIT, which would be -- presumably have been submitted by
4 them.

5 Gary.

6 PANEL MEMBER BYUS: Craig. Or Gary. Who do you
7 want?

8 CHAIRPERSON FROINES: You see, Alzheimers comes
9 on slow and --

10 PANEL MEMBER BYUS: I really do agree with you.
11 I mean I find the model very, very interesting. I think
12 it is a good -- it's a hypothesis model. I mean it's
13 based on very sound science, and it's laid out in a very
14 nice way. The problem is it hasn't really been validated
15 sufficiently, is my feeling.

16 I mean the linear dose extrapolation for
17 carcinogen model that everybody uses -- we all use has
18 been -- was validated extremely well through many, many
19 years. And this is actually a very good model, and it
20 just hasn't been validated enough. It hasn't been tested
21 appropriately. And it needs some more experimental
22 validation before it can really be adopted. If it were --
23 for example, if this was shown to be sort of correct with
24 proliferation models and distribution for a number of
25 other chemicals, even though there would be no new data

1 for formaldehyde specifically, we would all say the model
2 had a significant higher level of validation, and we'd be
3 much more likely to agree with it in the context of a
4 formaldehyde risk assessment here. But since it hasn't
5 really been validated extensively, experimentally, it's of
6 limited use in terms of changing what we already know.

7 But I do find, with you, that it is really new
8 and it's a very nice model and it really needs a lot more
9 work. Somebody should work on it because it's very, very
10 interesting. And it may in fact be correct.

11 PANEL MEMBER FRIEDMAN: So to clarify, you're --
12 given that you see a lot of strength to this model, you're
13 not recommending that OEHHA necessarily be the ones that
14 perfect it, validate it, and so on?

15 PANEL MEMBER BYUS: No, not at all.

16 PANEL MEMBER FRIEDMAN: They should -- once it is
17 perfected, validated, so on, then they can consider using
18 it. But it's not -- we're not recommending that they have
19 to do that?

20 CHAIRPERSON FROINES: I was being very specific.
21 I was saying that this petition -- the material within
22 this petition as far as I'm concerned is not ready for
23 prime time based on Dale Hattis' evaluation.

24 And what I would say is that the industry should
25 develop the model further and address the issues that Dale

1 raises, and there are -- I don't want to go through all
2 the points in his document, but there are obviously the
3 nonlinearity -- using an MLE model as opposed to an upper
4 confidence limit. And Dale would argue that when you go
5 to the upper confidence limit, you're going to lose some
6 of that nonlinearity, and so on and so forth. We could go
7 through it.

8 So the point is I'm saying it's not ready for
9 prime time, but that I would urge them to pursue it
10 further, and that when --

11 PANEL MEMBER FRIEDMAN: Who's the "them" that
12 you --

13 CHAIRPERSON FROINES: The CIIT and the
14 formaldehyde industry.

15 PANEL MEMBER FRIEDMAN: Okay. We just need to
16 make really clear who "them" is.

17 CHAIRPERSON FROINES: And when -- but I would
18 also argue that formaldehyde would be a good compound for
19 OEHHA to look at in their tier 2 process, because they
20 have to look at -- 15 chemicals?

21 SUPERVISING TOXICOLOGIST MARTY: Right.

22 CHAIRPERSON FROINES: And so if you had new
23 information that had been submitted when you're doing the
24 tier 2 process, that one might consider incorporating that
25 into a new risk assessment. And so it seems to me that

1 we're describing a process that would be -- if George and
2 Melanie agree, that would be appropriate for down the road
3 looking at how some of the uncertainties in the model have
4 been evaluated.

5 PANEL MEMBER FRIEDMAN: May I just clarify that?

6 Well, let's say they then do this formaldehyde
7 assessment for SB 25 a year from now and there's been
8 no -- little or no progress on the things that need to be
9 done with this CIIT model. Are you still recommending
10 that they use it?

11 CHAIRPERSON FROINES: No. I'm not recommending
12 that they use -- I'm not recommending they change
13 anything. I think the burden is on the petitioner to come
14 back and respond to the questions that have been raised,
15 and then to -- and to the degree that they are responded
16 to, then it would seem appropriate for OEHHA to
17 incorporate them because they do represent a certain level
18 of sophistication that might be relevant.

19 PANEL MEMBER FRIEDMAN: Okay. Well, that's the
20 first clear statement that we're putting the onus on the
21 petitioner. I want to make that -- I think that should be
22 very clear.

23 CHAIRPERSON FROINES: Well, it's a -- I'm talking
24 about a staged process and -- a staged process. And that
25 the first step would be for the petitioner to take the

1 Hattis report and update their model appropriately, and
2 then OEHHA could later consider that when they took up
3 formaldehyde.

4 PANEL MEMBER BLANC: Maybe OEHHA could comment on
5 this. But I would assume -- maybe I'll just wait until
6 they -- maybe OEHHA could comment on this, but I would
7 assume that if a version of this theoretical modeling
8 approach appeared in the public peer review scientific
9 literature in a published form, you would, as with other
10 peer review studies, take it into consideration when you
11 review formaldehyde as other compounds and as part of the
12 SB 25 process. Isn't that correct?

13 SUPERVISING TOXICOLOGIST MARTY: Yes, we would
14 look at all available information.

15 PANEL MEMBER BLANC: But you weight peer review
16 published information somewhat more strongly than --

17 SUPERVISING TOXICOLOGIST MARTY: We do.

18 PANEL MEMBER BLANC: -- anecdotal or non-peer
19 reviewed or non-published or proprietary information?

20 SUPERVISING TOXICOLOGIST MARTY: We do.

21 CHAIRPERSON FROINES: Are you comfortable with
22 what I have proposed?

23 SUPERVISING TOXICOLOGIST MARTY: Yes. The only
24 qualifying thing that I think I better say is we -- under
25 SB 25 we need to revise our risk assessment methodologies

1 to incorporate considerations of age at exposure on
2 potency of carcinogens as well as non-carcinogens.

3 We're in the process of doing that document.
4 It's -- as soon as we're done with ETS, Stan, we'll be
5 working harder on more of that document.

6 And we're also required to develop -- or to go
7 back and look at 15 TACs per year under that statute.
8 What we wanted to do is have at least some of those 15
9 TACs done when we put out the risk assessment revisions
10 for public review.

11 Formaldehyde is a little more complicated, in
12 part because of this type of information. So I wanted to
13 avoid promising that the first batch of chemicals we look
14 at is going to include formaldehyde. I think we can say
15 that we'll try. But there are these unresolved issues
16 with the model. You know, if they don't get resolved,
17 we're not going to look at it until they do get resolved.
18 So I don't -- the timing might be a little bit
19 problematic.

20 CHAIRPERSON FROINES: Yeah, but I think that we
21 have to be responsive to the petition as well. Insofar as
22 if CIIT or, quote, "formaldehyde industry" comes back in,
23 having addressed a lot of the issues, then it does seem to
24 me that it's incumbent upon us to be responsive to that
25 additional input. So to sort of say this one's more

1 complicated so we won't take it up as one of the 15, I
2 don't -- I think that -- I think that you would need to be
3 responsive to the fact that a significant -- I mean this
4 is not trivial and an enormous amount of work has
5 obviously gone into it. And so I think one has to be
6 responsive to that.

7 PANEL MEMBER FRIEDMAN: Well, I agree with what
8 you say. But isn't your first priority in this SB 25
9 process to look at risk to children? And if they don't
10 consider formaldehyde as necessarily a greater risk to
11 children as 15 others, then you wouldn't put that in the
12 first 15, right?

13 PANEL MEMBER BLANC: Well, it actually was number
14 6, if I recall. It had just -- was just bumped out of the
15 top 5. So --

16 CHAIRPERSON FROINES: Remember that formaldehyde
17 was originally proposed as one of the top 5. And it was
18 the recommendation of this panel that moved it down
19 actually. And so that means as far as I'm concerned, and
20 I think this is what Paul is saying, is that formaldehyde
21 is still higher on the list than perhaps some other
22 chemicals might be. So it would be appropriate to take it
23 up.

24 SUPERVISING TOXICOLOGIST MARTY: It wasn't on the
25 basis of its carcinogenicity primarily however.

1 CHAIRPERSON FROINES: I understand. It was on
2 that paper from you know who.

3 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
4 SALMON: I think a subsidiary point is that we might well
5 take it up early in the reevaluation process, but that it
6 might take us a while to complete the reevaluation. So
7 you wouldn't necessarily expect to see a final OEHHA
8 reevaluation in the first crop of reports simply because
9 this task is of sufficient magnitude that it could take
10 quite a while.

11 CHAIRPERSON FROINES: Well, this process with
12 formaldehyde's taken quite a while. And so I think it's
13 going to take a while presumably for the industry to
14 respond to the Hattis questions and those raised by it.

15 PANEL MEMBER BLANC: Well, does that mean that it
16 will take industry longer to respond than it's taken the
17 Air Resources Board to respond to the 1991 designation?

18 CHAIRPERSON FROINES: I don't understand the
19 question.

20 PANEL MEMBER BLANC: Well, I mean -- I think
21 earlier you said that it was designated in 1991. And has
22 there actually been any regulatory action from the Air
23 Resources Board or any program for reduction exposure or
24 control of formaldehyde based on that?

25 CHAIRPERSON FROINES: As far as I know, there has

1 not been a control plan developed for formaldehyde up to
2 the present.

3 Janette.

4 ARB AIR QUALITY MEASURES BRANCH BROOKS: We're
5 currently in the process of developing a control measure
6 for formaldehyde. And it's focusing on composite wood
7 products, like plywood and particle board and medium
8 density fiberboard. And we've gotten -- we've surveyed
9 the industry. We're looking at the data. And we're
10 looking at the technologies and the emissions from the
11 Board itself and how those can be lowered. And that's
12 where we are right now. We haven't gotten to the step yet
13 where we're looking at regulatory concepts, but we're
14 getting close.

15 PANEL MEMBER BLANC: Because I think it is very,
16 very important that this discussion not be misinterpreted
17 by the Air Resources Board as any indication from the
18 scientific panel that there need to be any delay or
19 slowing in the ongoing process from the Air Resources
20 Board point of view. Again, reiterating what Dr. Froines
21 said, which is that there's nothing in the information
22 that's been presented that suggests that formaldehyde is
23 not a toxic air contaminant.

24 CHAIRPERSON FROINES: Now, Jim just gave me a
25 message that I actually don't think I want to follow,

1 because I think that the letter that I sent to Alan Lloyd
2 responding needs to reflect what we've just been
3 discussing.

4 Jim says the question before the panel is to make
5 a recommendation to the ARB Chairman, Allen Lloyd, about
6 whether the panel feels the information contained in the
7 petition warrants reconsideration of the original risk
8 assessment.

9 And I think that we could have a vote on that
10 specific question, but I don't think it's what we're
11 really talking about. I think we're saying -- we're
12 saying that there is new information that's perhaps not
13 ready for reconsideration, but we do think that, given --
14 if that new information were to be provided -- further
15 information were to be provided, then it would be
16 appropriate for OEHHA to look it up.

17 PANEL MEMBER GLANTZ: Well, I think -- I'd like
18 to sort of differ slightly. I think we should answer the
19 question "no," because that is the sort of bureaucratic or
20 legal question before us. And I think we should say that
21 there is not new information before us to warrant
22 reopening the risk assessment. I think that's clearly --
23 the answer to that is clearly no. And I think that's all
24 you need to write back to Lloyd.

25 I think that -- there is a transcript of this

1 meeting. I think people have -- several people have said
2 there's some very interesting new information there, it's
3 not sufficient to warrant reopening the risk assessment.
4 But I think we've made it fairly clear to OEHHA and to the
5 petitioners that if further information is developed and
6 fed into the process, it ought to be considered very
7 seriously. And I think that we've made it clear that we
8 think formaldehyde is a high priority for the next phase
9 of SB 25. So I think there isn't much more to say.

10 I think the letter back to Lloyd should be
11 dealing with this narrow legal question of do we think
12 that they put forward information to warrant reopening the
13 risk assessment. And I think the answer to that is "no."
14 But I think -- there is this transcript of this meeting.
15 I think the panel's been pretty clear. And I think OEHHA
16 has a history of taking what we say seriously. And I know
17 that the formaldehyde people are going to listen to what
18 you said. And I think that's all we need to do at this
19 point.

20 PANEL MEMBER FRIEDMAN: I would like to make a
21 motion that we do just what Stan said, just answer "no"
22 and refer to the transcript for discussion of our thoughts
23 about it.

24 CHAIRPERSON FROINES: Well, I just -- we'll take
25 the motion in a second. But can we have some further

1 discussion on the point before we get to the motion?

2 PANEL MEMBER FRIEDMAN: Oh. Well, I made --

3 CHAIRPERSON FROINES: Make the motion.

4 PANEL MEMBER FRIEDMAN: I just did.

5 CHAIRPERSON FROINES: Okay. What is the motion?
6 State it again.

7 PANEL MEMBER FRIEDMAN: That we send -- we answer
8 Mr. Lloyd's question, "No, we don't think that further
9 assessment" -- whatever the wording is --

10 PANEL MEMBER GLANTZ: I think that we should
11 answer the question. Or, here, I'll make the motion.

12 PANEL MEMBER FRIEDMAN: Whatever he said, what
13 should we do, the answer is no. But we should say that
14 there was a lot of discussion and we indicated our
15 thoughts, which we've indicated further work on the part
16 of the petitioner and possibly OEHHA.

17 PANEL MEMBER GLANTZ: Well, actually I would
18 suggest just writing a letter back saying, "No," and leave
19 it at that. Yeah, because I think the rest -- because the
20 transcript is there and the views --

21 CHAIRPERSON FROINES: I don't think that's being
22 very responsible. I think that -- I personally feel that
23 the evidence is very close to making the answer "yes" from
24 my standpoint, and that --

25 PANEL MEMBER GLANTZ: Right.

1 CHAIRPERSON FROINES: So I think to answer the
2 question "no" and stop is to -- it's not quite
3 appropriate --

4 PANEL MEMBER BLANC: I think there are two
5 separate issues. Maybe I can help solve this a little
6 bit. One is the question of: What does the finding of
7 the Scientific Review Panel need to consist of? And,
8 secondly, how should the finding be transmitted to the Air
9 Resources Board?

10 So I think that from the narrow point of view
11 there needs to be a resolution passed by the Committee,
12 which I would propose in the following wording: The
13 Scientific Review Panel does not find that there is
14 sufficient new scientific data on the part of the
15 petitioner to require reopening of the previous risk
16 assessment by OEHHA. That's the resolution.

17 You should accompany the transmission of that
18 resolution with a text letter which summarizes some of the
19 discussion and some of our recommendations and refers to
20 the transcript. And I think that would be fine.

21 But I don't think we need to embody in a formal
22 resolution other aspects. My only clarification would be
23 that -- what I would suggest that you put also in the text
24 of the letter is that, in essence, the Committee -- in
25 coming to this conclusion the Committee felt that the

1 response of OEHHA to the petitioner had scientific merit.
2 Because part of our Scientific Review Panel is we're
3 commenting back on whether, you know, appropriate science
4 was used on OEHHA's part in their activities.

5 So there was a scientific approach by OEHHA to
6 the petitioner's information, reviewing it. And they came
7 back with comments. And there may be difference in nuance
8 of view on those comments, but I don't think we're seeing
9 anything inappropriate about the scientific approach of
10 OEHHA in evaluating the petition and responding to it.
11 And I think that does need to be in our resolution
12 perhaps. But I think the text of your letter should also
13 reemphasize that.

14 So I don't know if you got the wording to my
15 proposed resolution. Or, Peter, did you manage to write
16 that down?

17 PANEL MEMBER GLANTZ: Well, I think the intent
18 here is to -- I mean, as I said and I think what Paul
19 said, is I mean I think there's two separate issues that
20 are getting kind of confounded here. One is answering the
21 fairly -- the specific legal question that's been put
22 before us about whether or not the risk assessment
23 should -- enough evidence has put before us to reopen the
24 risk assessment. And I just think the answer -- and I
25 think that's what the letter should say. But I think we

1 have clearly indicated to OEHHA and to the petitioners
2 sort of a path to follow in the future. And in terms of
3 further sophistication of the model and the other
4 evidence, should the formaldehyde people want to bring
5 that forward --

6 PANEL MEMBER BLANC: So, Stan --

7 PANEL MEMBER GLANTZ: -- and we've also said to
8 OEHHA they ought to be considered seriously. So --

9 PANEL MEMBER GLANTZ: So, Stan -- so you don't
10 agree with my compromise suggestion?

11 PANEL MEMBER GLANTZ: Well, I don't see what
12 you're suggesting is that different from what I was
13 suggesting.

14 PANEL MEMBER BLANC: Well --

15 CHAIRPERSON FROINES: I think it's very
16 different.

17 PANEL MEMBER BLANC: What I'm suggesting -- well,
18 let me clarify what I'm suggesting. I worded a specific
19 resolution, which is actually now on the table and someone
20 can second if they want. And I'm deferring to the Chair's
21 discretion that in transmitting that resolution to the Air
22 Resources Board, that I think the Chair certainly would be
23 within his rights to also describe the context of that
24 decision and refer to some of the salient points of the
25 discussion as are reflected in the minutes of the meeting.

1 PANEL MEMBER GLANTZ: Well, I don't have a
2 problem with that. I think -- again, I don't -- I don't
3 have a problem -- John, if you think that it would be
4 useful or fair or anything else to describe some of the
5 discussion here in accompanying the decision, I don't have
6 a problem with that. I think there's one fairly specific
7 question we have an obligation to answer. And I think
8 everyone agrees that the answer to that question is no.

9 CHAIRPERSON FROINES: I don't think there's -- I
10 do not agree with you.

11 PANEL MEMBER GLANTZ: You don't think --

12 CHAIRPERSON FROINES: I don't -- I won't vote
13 because I'm the Chair. But I think that the -- I don't
14 think it's clear that there is not sufficient new evidence
15 to warrant a reevaluation of the risk assessment. I've
16 been clear on that. I think there is work to be done to
17 look at that issue further. But I think that there is new
18 information and I think that -- I'm not even clear that
19 OEHHA has taken -- I mean what is OEHHA's position? Is it
20 your position that there is not sufficient information to
21 warrant reopening? Is that your position?

22 SUPERVISING TOXICOLOGIST MARTY: That is our
23 position.

24 CHAIRPERSON FROINES: That is your position.

25 Well, people -- like-minded people can disagree.

1 So it's something -- we're going to take a vote on the
2 issue. But I don't -- I think it's important that if we
3 vote no, that we also give it a context, because as far as
4 I'm concerned I couldn't accept saying just no.

5 PANEL MEMBER GLANTZ: Well, no -- and I don't --

6 PANEL MEMBER BLANC: But that's what I'm
7 suggesting.

8 CHAIRPERSON FROINES: I understand that's what
9 you're suggesting. I'm talking to Stan.

10 PANEL MEMBER BLANC: But I think Stan's agreed
11 with what I suggested.

12 PANEL MEMBER GLANTZ: Yeah, well, I mean -- and I
13 don't object to that either. I mean the way I interpret
14 the discussion is that at this point on the table in front
15 of us right this moment there is not sufficient evidence
16 to warrant reopening the risk assessment. There are some
17 very intriguing information. There's some interesting
18 information. There is some information that if there is
19 further development of the models, further validation of
20 the models, sensitivity analysis, et cetera, et cetera,
21 then at some point in the future they might be able to
22 come back and present a better developed case that would
23 in fact lead the panel to say yes.

24 So I think in saying no we're not saying, "This
25 is the most ridiculous thing we've ever seen in our lives.

1 Go away and stop bothering us." I think we're saying
2 right now we don't have enough information. But, as I
3 said, I think that the transcript clearly outlines the
4 areas that we fell short and clearly outlines a sort of
5 road map for moving forward.

6 CHAIRPERSON FROINES: That's fine.

7 PANEL MEMBER GLANTZ: And I think that's -- and I
8 think that the petitioners, who seem highly motivated on
9 this, you know, I would expect will take what's in the
10 transcript and try to deal with it. I think we've said to
11 OEHHA that we think dealing with formaldehyde should be a
12 high priority. They don't seem to disagree with that.
13 And I think we've said that if better -- if the sort of
14 preliminary information that's been put before us is more
15 thoroughly developed and fleshed out to the point where --
16 you know, where people are a little bit more confident,
17 then they ought to consider it. But I think the record's
18 pretty clear on it.

19 CHAIRPERSON FROINES: Okay. I think that -- I
20 mean my view is that there is new evidence, but it's not
21 sufficiently developed and so we're -- we're in a gray
22 zone. So I would agree with the notion to say no, but
23 also I want to be able to say that there is interesting
24 information that requires further development.

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

1 that.

2 CHAIRPERSON FROINES: And I also think that this
3 panel should say explicitly to OEHHA that were the
4 information to be developed further, then we would expect
5 to see one as one of the 15 compounds next year. Melanie
6 kind of was a little wishy-washy on that issue. And I
7 think we should be explicit about it. I think we should
8 say formaldehyde should come up as one of the 15, because
9 there is -- this isn't -- this is not a trivial situation.
10 We do have a fairly major degree of work that's been
11 provided that should be taken quite seriously.

12 PANEL MEMBER GLANTZ: I don't think anybody's
13 disagreeing with that. I didn't think Melanie -- I didn't
14 think Melanie said one --

15 CHAIRPERSON FROINES: Well, she was a little --
16 Joe.

17 PANEL MEMBER GLANTZ: What do you, Melanie --

18 CHAIRPERSON FROINES: No, no, no, no. We don't
19 have to get -- no, we're back with Joe.

20 PANEL MEMBER LANDOLPH: Just, you know, from my
21 own point of view. Again, it's an intriguing model. It's
22 intellectually interesting. It's got a lot of cell
23 division and mutation rates. But there are some things in
24 it I think a lot of us are not comfortable with. The
25 nonlinearity between .5 and one parts per million, which

1 is the relevant dose, where the risk goes up a hundred
2 fold. That's worrisome. I don't know what that means,
3 and that and this great influence of the cell division
4 parameters on it. So I'm not convinced the model is
5 anywhere near settled yet. It needs a lot more
6 developmental work.

7 CHAIRPERSON FROINES: There's no question about
8 that. The CIIT position has, since the late seventies,
9 viewed the cancer risk assessment data consistently, that
10 they really believe that as you go from 1 up to 5 up to
11 15, that -- that what really is going on is cytotoxicity
12 and cell replication, as we all know. And that's the
13 driving ideological feature. But it's not that simple,
14 and that's what we're asking them to look into more
15 carefully.

16 Kathi.

17 PANEL MEMBER HAMMOND: What I'm hearing -- excuse
18 me. There are two issues -- two reasons that the petition
19 should be considered. And one is this new epidemiology
20 evidence, one is the model.

21 And we've been talking about -- I think it was
22 clear from what Gary said, that -- but I just want to get
23 some clarity here -- that there's not sufficient new
24 evidence from the epidemiology to reopen the
25 consideration. So we're really just talking about the

1 model. And it seems to me from what I've been hearing
2 from everybody speaking about this that the model is
3 insufficient at the moment to reopen the consideration.
4 However, the model is intriguing and so we would want to
5 encourage OEHHA to become familiar with the model, to be
6 looking at it. Not to say, "Oh, well, we don't need to
7 look at it now because the Scientific Review Panel said
8 that we don't need to reopen formaldehyde."

9 So I guess what I'm hearing, but maybe I'm
10 missing something here, is that the petition itself
11 should -- we would not be supportive of it on the basis of
12 a model either because the model's not sufficient yet to
13 reopen. But we do think -- and then the burden lies with
14 CIIT to further develop and validate the model to make it
15 sufficient to reopen. The specific concerns about the
16 model have been mentioned both by Dale Hattis and by Dr.
17 Landolph. But we do think that OEHHA should be paying
18 attention to this model and looking at it in more detail.

19 CHAIRPERSON FROINES: Is there a second to Paul's
20 resolution? Because you said --

21 PANEL MEMBER GLANTZ: Okay. I'll second.

22 I'll withdraw mine or --

23 CHAIRPERSON FROINES: What you said and what Joe
24 said and -- I've lost track. But I think there is a
25 general consensus among the panel. So I think we should

1 move to voting, unless there's -- unless we're going to
2 start repeating ourselves.

3 PANEL MEMBER FRIEDMAN: Was it stated when I was
4 out of the room? I'd like it -- I was out of the room for
5 a couple of minutes.

6 CHAIRPERSON FROINES: Well, we never go back.

7 PANEL MEMBER BLANC: I simply word it -- yeah.

8 PANEL MEMBER FRIEDMAN: You said that we'd say
9 no, but the Chairman has the prerogative to explain --

10 PANEL MEMBER BLANC: That's not part of the
11 resolution. But I also said that it was the sense of the
12 Committee that the Chair certainly had the prerogative to
13 place this in a letter in context. That's not part of the
14 resolution. The resolution is as I stated it. I don't
15 think people need to have it read back. And I heard Stan
16 second.

17 I wonder if someone would like to call the
18 question.

19 CHAIRPERSON FROINES: Is there discussion?

20 PANEL MEMBER BYUS: Just one more point, john.

21 CHAIRPERSON FROINES: Sure.

22 PANEL MEMBER BYUS: I'm very intrigued by the
23 model. It's a very good hypothesis. Hattis has very good
24 criticisms of the model based on certainty, et cetera.
25 But I think it needs to be experimentally verified, not

1 just dealt with mathematically in terms of degrees of
2 uncertainty. It needs to be done experimentally. We need
3 to see some data verifying the validity of the model,
4 particularly this nonlinearity flux point.

5 Now, how that is to be done, I could make a
6 variety of suggestions. But that's not likely to be done
7 in like six months or a year. But the model is a good one
8 and it just -- and it gets the mathematical concerns the
9 degrees of uncertainty needs to be dealt with and all the
10 things that Dale Hattis suggested is the expert. But we
11 need to do some experiments to provide some data to show
12 that the model is in fact predictive. That's -- and that
13 is likely to take a reasonably long time to do. So I just
14 wanted to make that clear.

15 CHAIRPERSON FROINES: That's not an entirely
16 trivial --

17 PANEL MEMBER BYUS: No, it is not trivial. But
18 this model is intriguing enough that if it had some
19 experimental backup, it could be adopted. But if it
20 doesn't have the experimental data it's -- to my point of
21 view is less likely to be --

22 CHAIRPERSON FROINES: Well, I think there -- to
23 the degree that they addressed what Hattis has suggested,
24 that we -- we might then agree to dis -- I mean for some
25 of us it might be sufficient, for others it might not.

1 And so that's something to take up at a later time.

2 PANEL MEMBER BYUS: That's fine.

3 CHAIRPERSON FROINES: I think that -- I do think
4 that -- the one thing that worries me about taking up new
5 mathematical modeling is that you can open the proverbial
6 Pandora's Box and everybody and his brother will start
7 petitioning --

8 PANEL MEMBER BYUS: Without experiments --

9 CHAIRPERSON FROINES: And so the greater the
10 validation of data -- new data, the better off I think is
11 a general principle.

12 PANEL MEMBER BLANC: So it seems like we have
13 come to consensus. I think it would be useful to call the
14 question.

15 PANEL MEMBER FRIEDMAN: I'm sorry. I really
16 would like to hear what we're voting on.

17 PANEL MEMBER BLANC: Could you read back.

18 CHAIRPERSON FROINES: Say it again.

19 PANEL MEMBER BLANC: Resolved that the Scientific
20 Review Panel finds that there is not sufficient new
21 scientific data to support the petition to formally reopen
22 the prior risk assessment on formaldehyde.

23 PANEL MEMBER FRIEDMAN: Thank you.

24 CHAIRPERSON FROINES: And you understand that
25 there's another proviso which is -- it's not part of the

1 motion?

2 PANEL MEMBER BLANC: And I'll say that again
3 afterwards. Let's vote on the motion first.

4 CHAIRPERSON FROINES: Are we ready to take the
5 question?

6 All those in favor.

7 (Hands raised.)

8 CHAIRPERSON FROINES: It's unanimous.

9 PANEL MEMBER BLANC: Then I would like the
10 minutes to reflect the consensus of the panel that it
11 should be the Chair's prerogative in transmitting this
12 resolution to the Air Resources Board to summarize the
13 discussion that occurred and the context in which this
14 decision was made both in terms of what further work on
15 the model might be done as well as what priority OEHHA
16 should place on formaldehyde in its SB 25 follow-up.

17 CHAIRPERSON FROINES: We don't need to vote.

18 PANEL MEMBER BLANC: No, as long as --

19 CHAIRPERSON FROINES: Stan, this is a tricky
20 issue. You had apparently significant comments on silica,
21 and you're about to walk out the door.

22 PANEL MEMBER GLANTZ: Right. But I'll call back
23 in at 1:30.

24 CHAIRPERSON FROINES: Well, should we take up
25 then something else before --

1 PANEL MEMBER GLANTZ: I would suggest that.

2 CHAIRPERSON FROINES: Where's Jim?

3 Jim, is this going to work with Stan calling in?

4 MR. BEHRMANN: I think -- they claim so.

5 CHAIRPERSON FROINES: So 1:30.

6 PANEL MEMBER GLANTZ: I'll call back about 1:30.

7 CHAIRPERSON FROINES: So we'll hold off silica
8 till 1:30.

9 PANEL MEMBER GLANTZ: Okay. I'm sorry.

10 CHAIRPERSON FROINES: That means we miss Gary.

11 So it's -- I guess we have to make a decision
12 about which one --

13 PANEL MEMBER GLANTZ: You could discuss it with
14 Gary, and then I could call in later. But I've got --

15 PANEL MEMBER FRIEDMAN: I don't have strong
16 feelings about it. So --

17 CHAIRPERSON FROINES: Stan, do you have strong
18 views? Would you -- I mean is it important for you to
19 be --

20 PANEL MEMBER GLANTZ: I can just quickly say for
21 the record if you want --

22 CHAIRPERSON FROINES: No, no, no, no, no.

23 PANEL MEMBER GLANTZ: Well, no. What it is --
24 and then I do have to run.

25 CHAIRPERSON FROINES: I don't think this is going

1 to work.

2 PANEL MEMBER GLANTZ: What, for me to call in
3 later?

4 CHAIRPERSON FROINES: For you to make now a
5 two-minute presentation.

6 PANEL MEMBER GLANTZ: Okay. I think I'll just
7 call in and I can listen to the presentation. There have
8 been some specific statistical issues about silica that
9 I've looked at. I've had several discussions with OEHHA
10 about them. And we'll just discuss them in the context of
11 the presentation.

12 CHAIRPERSON FROINES: Is one of those issues the
13 Berry comment -- most recent comments, I hope?

14 PANEL MEMBER GLANTZ: Yeah. Is that the one
15 about the life table versus --

16 CHAIRPERSON FROINES: Yes.

17 PANEL MEMBER GLANTZ: Yeah, that's right.

18 CHAIRPERSON FROINES: Your input would be very
19 valuable on that.

20 PANEL MEMBER GLANTZ: Okay. So that's --

21 CHAIRPERSON FROINES: So 1:30 then.

22 PANEL MEMBER BLANC: Out of deference to our
23 stenographer, can we have a break?

24 CHAIRPERSON FROINES: Can we take a ten-minute
25 break.

1 (Thereupon a recess was taken.)

2 CHAIRPERSON FROINES: Let's move ahead. He'll be
3 here momentarily.

4 Naphthalene.

5 SUPERVISING TOXICOLOGIST MARTY: Okay. The next
6 item is discussion of the unit risk factor for
7 naphthalene.

8 To my left is Dr. Joe Brown. He will be giving a
9 presentation first on why we are looking at naphthalene
10 and then on what we did to develop a unit risk factor.

11 Joe.

12 (Thereupon an overhead presentation was
13 Presented as follows.)

14 STAFF TOXICOLOGIST BROWN: Thank you, Melanie.

15 I have a few background slides to start with
16 here.

17 --o0o--

18 STAFF TOXICOLOGIST BROWN: The first slide gives
19 a little bit of background on the regulations naphthalene
20 fall under: Toxic Air Contaminants Act, AB 1807; the Air
21 Toxics Hot Spots, AB 2588; and also naphthalene as a PAH
22 would probably also fall under SB 25.

23 --o0o--

24 STAFF TOXICOLOGIST BROWN: Structure naphthalene.

25 This is the structure of naphthalene.

1 Naphthalene is a toxic air contaminant based on two
2 criteria: It's a federal hazardous air pollutant, or an
3 HAP, under the U.S. Clean Air Act of 1990. And,
4 therefore, it's a TAC is a single substance. It's also a
5 member of the class Polycyclic Organic Matter, POM. POM
6 is separately a HAP and a TAC.

7 --o0o--

8 STAFF TOXICOLOGIST BROWN: Industrial emissions
9 of naphthalene are reported to be 360,000 pounds in 1997.
10 Primary source is probably vehicle exhaust. Also occurs
11 in wood burning. And it's a component of environmental
12 tobacco smoke. The 12-hour average ambient air
13 concentrations range from 348 to 715 nanograms per cubic
14 meter in 1994 in California.

15 This is data from Atkinson in 1995.

16 --o0o--

17 CHAIRPERSON FROINES: Can I just make one comment
18 about that, Joe?

19 STAFF TOXICOLOGIST BROWN: Sure. Go ahead.

20 CHAIRPERSON FROINES: First is we've been -- we
21 have sampled for naphthalene across 12 different
22 communities in the Los Angeles basin, and we find values
23 up to 6,000 nanograms per cubic meter. Distribution is
24 very skewed.

25 And I should say for the panel that may not be

1 aware of this. If you compare the -- in Riverside, for
2 example, where Craig's from, the average that we measure
3 is around 580-600. But the point I wanted to make is that
4 the level of benzopyrene, which gets most of the attention
5 in this field, is around 100 picograms per cubic meter.
6 So it's about -- in terms of our values, we tend to find
7 that naphthalene is somewhere between 5,000 and 50,000
8 times greater than any other PAH that we see in the Los
9 Angeles basin. So it's quite a dramatic exposure issue.

10 PANEL MEMBER HAMMOND: And just, you know, to add
11 to that, we've been doing measurements in Fresno and
12 seeing very similar results.

13 STAFF TOXICOLOGIST BROWN: It's a problem.

14 PANEL MEMBER HAMMOND: Yeah, year-round
15 measurements there, too.

16 STAFF TOXICOLOGIST BROWN: This slide gives a
17 little background on the non-cancer health effects.
18 Respiratory effects seen in mice. Damage to the
19 respiratory tract, including inflammation, epithelial
20 changes, damage to ciliated and Clara cells of the
21 bronchiolar epithelium, with neonatal mice being more
22 sensitive.

23 There's also a report on hemolysis and
24 methemoglobinemia in infants exposed to high doses of
25 naphthalene. This was not by inhalation, but by oral and

1 dermal route.

2 --o0o--

3 STAFF TOXICOLOGIST BROWN: There is a chronic
4 inhalation reference exposure level, or cREL, for
5 naphthalene established by OEHHA in 2000 of nine
6 micrograms per cubic meter, or two parts per billion,
7 based on respiratory effects in mice: Nasal inflammation,
8 olfactory epithelial metaplasia, and respiratory
9 epithelial hyperplasia.

10 --o0o--

11 STAFF TOXICOLOGIST BROWN: Carcinogenicity.
12 There's an NTP 1992 study -- inhalation study in mice,
13 giving some evidence -- that was the official
14 conclusion -- of lung tumors in female mice.

15 NTP ran an inhalation study in rats in 2000. And
16 this study showed clear evidence of respiratory epithelial
17 adenoma in male and female rats; and olfactory epithelial
18 neuroblastoma, a rare tumor, in male and female rats.

19 IARC in 2000 reclassified naphthalene as Group
20 2B, possibly carcinogenic to humans. Other relevant data
21 include genetic toxicity. Studies in bacteria are
22 generally negative. Studies in some mammalian cells are
23 positive.

24 --o0o--

25 STAFF TOXICOLOGIST BROWN: These are the bioassay

1 results of -- a summary slide of them. Across the top
2 here you can see the concentrations used. These are
3 generally six hours per day, five days per week. Here we
4 have the results of the mouse study from 1990. Lung
5 alveolar and bronchiolar adenomas and carcinomas. These
6 are the quantal responses, the control, and the test
7 concentrations.

8 The P values in this column here are the trend --
9 significance value for the trend test. And values for
10 pairwise comparisons are given under the individual
11 exposure levels, significance for that level versus the
12 control.

13 So as you can see in the mice, we have a
14 significant trend, but only a significant effect at the
15 top dose.

16 Moving down to the female rats. The two nasal
17 tumors, the nasal respiratory epithelial adenoma in the
18 top row here, given a quantal response. Significant trend
19 and significant effects across the board in pairwise
20 comparisons.

21 And for the nasal olfactory epithelial
22 neuroblastoma, there's a significant trend, but only a
23 significant pairwise comparison in the mid dose.

24 For the female rats the nasal olfactory
25 epithelial neuroblastoma gave a trend test, but only a

1 significant effect in the top dose. I should point out
2 here that the numerators we use in these studies are
3 generally the animals at risk. We don't include those
4 animals that died before they had a chance to get the
5 tour.

6 --o0o--

7 STAFF TOXICOLOGIST BROWN: Now, the dose response
8 methods we used were the linearized multistage model in
9 the guidance we issued in 1985. This is a q1* by the
10 MSTAGE -- in the MSTAGE program published by Crouch in
11 1992.

12 We also used the LED10 method put forward by the
13 U.S. EPA in their 1996 proposed cancer guidelines and the
14 latest version of their software to use this method, the
15 Benchmark Dose Software version 1.3.2 of 2002.

16 We also used a multisite potency, a Monte Carlo
17 method for combining two of the nasal tumors -- individual
18 tumor potencies into a combined value.

19 We used interspecies scaling, body weights of
20 human over body weight animal to the one-third power. And
21 this factor was applied to the potency.

22 --o0o--

23 STAFF TOXICOLOGIST BROWN: We use these
24 inhalation elemetric relations to estimate the amount of
25 naphthalene inhaled during the bioassays. The body

1 weights for the mice here and the rats were the
2 time-weighted average body weights over the course of the
3 bioassay.

4 And we assumed that inhalation uptake was equal
5 in all species. We didn't have sufficient information
6 really to differentiate that. We did look at potential
7 pharmacokinetic differences and we didn't identify any.

8 --o0o--

9 STAFF TOXICOLOGIST BROWN: This slide summarizes
10 the potency values and the goodness of fit test for the
11 multistage method analysis. You can see here, in the
12 first column we have the animal potency in terms of per
13 milligram per kilogram died, the human value based on the
14 scaling, the human unit risk in terms of milligrams per
15 meter cubed -- per milligram per meter cubed, and the
16 goodness of fit statistic. And this statistic, the
17 criteria was a value that equaled or exceeded .1 on a chi
18 square goodness of fit test.

19 And here we have the various end points that we
20 looked at: The female mice tumors and the various male
21 rat nasal tumors; the combination of the male rat tumors,
22 which is bold faced here because this is the value we
23 actually used in the end, the 0.34 is the key value. But
24 also we have the female nasal epithelial neuroblastoma
25 value here on the bottom. They're all highly significant

1 good fits.

2 --o0o--

3 STAFF TOXICOLOGIST BROWN: If you look at the
4 next table, this is the result of the parallel LED10
5 analysis. And the values are almost identical. In this
6 column we have the LED10; the human potency; the human
7 unit risk value, where we had .034, by the multistage we
8 had .031 by using this method. So they're virtually
9 identical. And the fits are also excellent.

10 --o0o--

11 STAFF TOXICOLOGIST BROWN: This just gives a
12 picture of the LED10 methodology, which some of you may
13 not be familiar with. The object here is to fit the
14 observed data to any one of a series of dose response
15 models. In this case, we use a quantal linear model.

16 And the critical values here are the 10 percent
17 effect left, which is shown here, 10 percent over the
18 background, and the lower bound on that level here. So in
19 this case the unit risk -- and this was the dose in parts
20 per million and the fraction of having tumors. Unit risk
21 would simply be the slope of the line drawn between this
22 point here -- and to keep my hand steady -- and the
23 origin, or simply this value divided by this value here,
24 which would be the slope of that line. Plus various
25 correction factors would be added onto that.

1 --o0o--

2 STAFF TOXICOLOGIST BROWN: Summary is that using
3 either methodology, the 95 percent upper confidence bound
4 on the unit risk value is in the range of .014 to .034 per
5 milligram per meter cubed based on tumor incidence data
6 and female mice and male and female rats from the NTP 1992
7 and 2000 studies.

8 The male rat was the most sensitive sex and
9 species tested. And the NTP considered the rare nasal
10 tumors to provide clear evidence of carcinogenicity for
11 naphthalene. The potency and unit risk values for the
12 combined nasal tumors are considered the best values for
13 the purpose of risk assessment.

14 --o0o--

15 STAFF TOXICOLOGIST BROWN: And on the next slide
16 I summarized these values.

17 For the naphthalene unit risk and units of
18 milligrams per cubic -- per milligram per cubic meter,
19 .034 or 3.4×10^{-5} per microgram per cubic meter or
20 0.12 per milligram per kilogram per day.

21 The predicted risk at the high value noted by
22 Atkinson here in 1995 would even be higher, based on Dr.
23 Froines' statement, of 715 nanograms per cubic meter would
24 be 2.4×10^{-5} lifetime risk.

25 SUPERVISING TOXICOLOGIST MARTY: We're going to

1 stop right here. That's all we have for summarizing what
2 we did. We do have more slides touching on the key
3 comments that we received during the public comment period
4 and our responses.

5 CHAIRPERSON FROINES: Why don't you go ahead with
6 those.

7 SUPERVISING TOXICOLOGIST MARTY: Okay.

8 --o0o--

9 STAFF TOXICOLOGIST BROWN: Okay. The first
10 comment summarized, the commenter objected to the
11 adjustment of the numbers at risk for the early deaths in
12 the bioassay results.

13 Our response was this is an appropriate method
14 and also standard procedure according to OEHHA cancer risk
15 assessment guidelines. The fact is we've been doing this
16 for years, and I don't -- you know, we're sort of
17 surprised at this comment actually.

18 PANEL MEMBER BLANC: Well, didn't you also make
19 the point that this is also standard not just for you guys
20 but EPA and everybody else?

21 STAFF TOXICOLOGIST BROWN: Yes. And also you get
22 a better fit to the data if you do this.

23 PANEL MEMBER BLANC: No, I'm just saying I
24 thought that was a convincing response.

25 --o0o--

1 To our way of thinking you need to really prove a
2 nonlinear approach. The default is the approach we've
3 taken basically. And I don't -- I mean we haven't been
4 shown data that convinces us that the approach is
5 nonlinear. I know that's open for discussion.

6 PANEL MEMBER BLANC: Can you clarify something
7 that confused me in the argument made in at least one of
8 the submitted comments --

9 STAFF TOXICOLOGIST BROWN: I'll try.

10 PANEL MEMBER BLANC: -- which seemed to go --
11 maybe I misinterpreted the argument, but it was almost as
12 if the argument was that it was genotoxic but not
13 mutogenic and, therefore, it shouldn't be a nonlinear
14 factor. I mean there was a lot of hand waving about how
15 the mutogenicity data were equivocal in certain assays but
16 that -- and then they cited as support of that that it
17 seemed to induce chromosomal abnormalities without being
18 mutogenic in mutogenicity assays and, therefore, it wasn't
19 genotoxic.

20 And I wondered -- it seemed to be a somewhat
21 confusing use of the language. And it would be useful for
22 me to hear from OEHHA's point of view -- I would assume
23 that you would approach something which caused chromosomal
24 abnormalities as being genotoxic whether or not you could
25 show it was mutogenic.

1 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

2 SALMON: We do actually --

3 STAFF TOXICOLOGIST BROWN: I agree.

4 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

5 SALMON: We do actually have some slides in a minute which
6 we can -- where we can talk a little bit more about the
7 genotoxic data. But certainly OEHHA's position is that,
8 you know, these various kinds of endpoints all represent
9 some form of genotoxic hazard and would be, you know,
10 considered as evidence on the side of presuming a
11 genotoxic mechanism for the purpose of the low dose
12 extrapolation here.

13 As to the argument about -- in the comment, I
14 must admit if I could figure out exactly what it was they
15 were proposing, I would probably disagree with it. But --

16 PANEL MEMBER BLANC: Well --

17 SUPERVISING TOXICOLOGIST MARTY: I think it's
18 important to note that in terms of assays for
19 genotoxicity, you don't weight them all the same because
20 they aren't actually measuring all of the same thing in
21 terms of the mutation produced. So it's a false argument
22 to say, "Well, we have, you know, ten negative studies and
23 five positive studies. Therefore, it is not genotoxic."

24 PANEL MEMBER BLANC: That was only part of their
25 argument. But the other -- wasn't there a part of their

1 argument was implying that it wasn't mutogenic; and,
2 granted, it is genotoxic; but, therefore, because it's
3 genotoxic but not mutogenic, you should do something
4 different? Didn't they themselves in their own argument
5 describe it as being genotoxic?

6 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

7 SALMON: Yes. And I think we -- and we disagree with the
8 premise behind that argument.

9 PANEL MEMBER BLANC: So one of the things that I
10 did think about, that OEHHA's reply perhaps to their
11 criticism was that you could have even made the same
12 argument that you made even stronger. I'm not undermining
13 your rejection of their argument. But I thought that
14 there was some more fatal flaw in their reasoning that
15 didn't quite come through as strongly in your reply as
16 could have been. But maybe I'm the only one who read it
17 that way.

18 John, did you -- I mean you're near knee deep in
19 this stuff. So did you --

20 CHAIRPERSON FROINES: I'm going to comment on it
21 in a few minutes at some length. So we don't need to --
22 I'd rather give a longer presentation than to sort of deal
23 with it in this context.

24 PANEL MEMBER LANDOLPH: I think this is rather
25 straightforward. I think they were trying to define

1 clastogenic as nongenotoxic. To me genotoxic is an
2 all-encompassing term. But clastogenic fits in there.
3 And if this clastogenic, then it is genotoxic and then
4 there is a linear no-threshold dose response curve, unless
5 they can provide strong evidence to the contrary. And
6 there is no evidence to the contrary for existence of a
7 threshold whatsoever.

8 STAFF TOXICOLOGIST BROWN: Right, and that that's
9 the only mechanism.

10 PANEL MEMBER LANDOLPH: And that's the argument,
11 I think. So I think they're mixing -- they're not using
12 the language properly, I think, is what I sensed.

13 PANEL MEMBER BLANC: Okay. Good.

14 So I didn't -- it's not something that I missed.
15 Because when I read it I thought, "Wait, am I" -- you
16 know, did something pass me by, did I sleep through that
17 lecture or -- you know that feeling that you have? Okay.

18 --o0o--

19 STAFF TOXICOLOGIST BROWN: This slide just
20 summarizes some of the metabolism on naphthalene. It's
21 not surprising that it forms epoxides, diol epoxides,
22 quinones, types of chemistry similar to other carcinogenic
23 polycyclic aromatic hydrocarbons. So it's not implausible
24 at least based on metabolism that something like this
25 could be a genotoxic carcinogen at least based on

1 metabolic considerations.

2 --o0o--

3 STAFF TOXICOLOGIST BROWN: This is a summary
4 slide of the genotoxicity showing the individual assays
5 and the results. You know, there are a bunch of
6 negatives, there are some positives. I don't know if you
7 want to comment on specific tests.

8 --o0o--

9 STAFF TOXICOLOGIST BROWN: There's also a few
10 results on some of the metabolites, also positive results
11 and negative results. It's a bit of a mixed bag. I don't
12 know if you can take this and prove a nonlinear mechanism.
13 Frankly, I don't think you can.

14 PANEL MEMBER LANDOLPH: Could you go back one
15 slide for a second please.

16 STAFF TOXICOLOGIST BROWN: Sure.

17 This is without or with observation?

18 This is our IT.

19 PANEL MEMBER BLANC: Can you comment on whether
20 or not the microsomal-enzyme-added salmonella test results
21 are consistent with the salmonella mutogenicity on the
22 next slide of the metabolite -- is, therefore, this --
23 yeah --

24 STAFF TOXICOLOGIST BROWN: They're only
25 negatives.

1 PANEL MEMBER BLANC: No, the 1,2 -- the
2 1,2-naphthoquinone --

3 STAFF TOXICOLOGIST BROWN: -- metabolite is
4 positive.

5 PANEL MEMBER BLANC: Is positive?

6 STAFF TOXICOLOGIST BROWN: Yes.

7 PANEL MEMBER BLANC: Is the 1,2-naphthoquinone
8 not a metabolite that would be generated by the microsomal
9 enzyme?

10 STAFF TOXICOLOGIST BROWN: Well, let's see. The
11 naphthoquinone would be up in here. Let's see if I can
12 point this out.

13 Right here. That's it right there.

14 PANEL MEMBER BLANC: I'm just trying to
15 understand biologically why it wouldn't have -- but the
16 only interpretation of why it's not positive in the Ames
17 test as the parent compound is that the liver microsomal
18 enzymes don't metabolize it to this limit?

19 STAFF TOXICOLOGIST BROWN: There's lots of
20 reasons for something to be negative. But when you find
21 something positive, you know, that's something I can
22 respond.

23 PANEL MEMBER LANDOLPH: Yeah, you have to be very
24 careful because when you're dealing with quinones you get
25 redox cycling. And Bruce Ames and his colleagues had to

1 devise a special strain to capture oxygen radical damage
2 in the first place. So that could be a very tricky issue,
3 you know, the detection sensitivity of the various
4 strains, because the reversion's very specific. So you
5 could miss something.

6 STAFF TOXICOLOGIST BROWN: I don't think we're
7 claiming we have a mechanism here. We're just claiming
8 plausibility.

9 PANEL MEMBER BLANC: I mean, yeah, that's
10 about -- the nature of my question is to plausibility,
11 because if there was a straightforward answer, which is
12 that the liver microsomal enzymes don't metabolize down
13 this pathway, therefore the quinone metabolite is not
14 produced in the Ames test unless you put in the
15 metabolized compound itself, it won't -- the parent
16 compound won't generate the metabolite question. Because
17 when they test in the same assay the metabolite, it was
18 positive for mutation.

19 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
20 SALMON: I think typically the conditions which you have
21 in the standard salmonella reverse mutation assay not
22 particularly conducive to picking up signals from this
23 kind of metabolite, as Joe said. So the fact that it
24 would be generated at perhaps rather simply low
25 concentrations by metabolism in the petri dish with S9

1 could -- you know, that could be missed.

2 Whereas, if you were basically putting a bucket
3 loadful directly in the actual assay in the metabolite,
4 then, you know, perhaps the less sensitive test strain is
5 adequate. But this is a common problem, as Joe was
6 saying, with detecting this kind of response.

7 SUPERVISING TOXICOLOGIST MARTY: That's all we
8 had.

9 CHAIRPERSON FROINES: Okay. I think that there
10 needs to be some points made about this -- about the
11 questions Paul's asking.

12 I think that this document -- I'm the lead from
13 that point.

14 One of the problems with this document isn't
15 anybody's fault. It's the fact that this is already a
16 TAC. So we're not developing a document for a TAC
17 determination. What we're doing is basically doing a risk
18 assessment. And so one could have a very brief document
19 that focuses on the risk assessment. I don't have any
20 problems with the risk assessment whatsoever. So as far
21 as I'm concerned, case done, the issue's over.

22 But I think that there is another issue here,
23 that I'm very sensitive to for a number of reasons. And,
24 that is, that I think in some respects it's important to
25 have some information on mechanism because that goes to

1 the issue of biological plausibility, which Paul's been
2 raising and Joe's commented on.

3 Now, in the first place we've done measurements
4 throughout the Los Angeles basin in 12 different
5 communities. And the first thing that one has to say is
6 we find naphthoquinone in every place we look in Los
7 Angeles. There is no place in all of southern California
8 where you don't find 1,2- and 1,4-naphthoquinone, period.
9 It's everywhere. And it comes from naphthalene.

10 So forgetting metabolism for a moment, we have to
11 control naphthalene in the environment because it's formed
12 when you combust fuel. So that naphthoquinone is always
13 going to be present. It's hot-tube chemistry. You take a
14 fuel and you put it in a hot tube and you produce
15 naphthoquinones because you take naphthalene and you add
16 oxygen as part of the combustion process, you get quinones
17 by definition.

18 And the second thing is we now know from some
19 work that's been published that if you take
20 nitronaphthalenes that are formed in atmospheric
21 chemistry, they degrade to naphthoquinones. If you
22 measure what happens with 1,4-naphthoquinone as you go
23 from the coast to Riverside, the amount of naphthoquinones
24 increases. In other words, we're forming naphthoquinones
25 from atmospheric processes.

1 And fourth, it's been known since the second
2 world war that naphthoquinones are a metabolite of
3 naphthalene. And I brought the papers to show it, that
4 this issue of the metabolism has been known since Louis
5 Fieser worked on naphthoquinone antibacterials during the
6 second world war. And there are papers on naphthalene
7 metabolism in 1953 in the biochemical journal. And so
8 that it's not as though this is a mystery science. This
9 has been something for which there have been dozens of
10 papers developed over the last 50, 60 years.

11 Now, if we started talking here about -- so
12 naphthalene ends up, in part at least, as naphthoquinone.

13 If we were talking about Butadiene, we would talk
14 about Butadiene for about two minutes and then we would
15 get into the mono and diapoxide because we would say the
16 carcinogenicity comes from the mono and diapoxide. And so
17 we wouldn't even bother to spend much time with Butadiene
18 because we know we have to talk about a metabolite.

19 But somehow with naphthalene we don't -- we get
20 to this issue of its metabolism late in the discussion as
21 though it's a mystery process. Well, it's not a mystery
22 process. It's a very well documented process.

23 So that we should be talking about the metabolize
24 of naphthalene almost immediately because it's the same
25 bio-transformation or atmospheric transformation. So

1 that's what I want to say.

2 Now, once having said that, the other thing
3 that's true is naphthoquinone binds with glutathione and
4 causes a DNA damage, and may be much more potent when it's
5 bound to glutathione. So that there are two toxic
6 elements that get formed. One is the glutathione
7 conjugate which can be excreted, but also is itself
8 capable of redox chemistry and electrophilic activity.

9 And so --

10 PANEL MEMBER BLANC: That's unusual, isn't it?

11 CHAIRPERSON FROINES: Well, not with quinones.
12 Quinones -- people should need to know more about
13 quinones, because they're ubiquitous and they don't get
14 enough attention, although they have supertoxicity.

15 So, anyway, they do do redox chemistry. But we
16 developed an assay from measuring the electrophilicity of
17 quinones. And it turns out in our assay that
18 1,4-naphthoquinone is the most electrophilic of the
19 quinones that we've measured so far. So you have
20 electrophilicity that is binding with thyols and DNA bases
21 as well as the redox activity that Joe's been talking
22 about.

23 So, bottom line, to answer your question,
24 naphthoquinone is genotoxic. And there's plenty of
25 evidence to show it. For example, here's a paper by --

1 there are -- Steve Rappaport, who we all know, has all
2 these albumin adducts that he's been looking at.

3 Here's a paper, it talks about a change in
4 function mutations in P53. That's a 2002 paper.

5 Here DNA strand scissions by quinone -- by the
6 same quinones.

7 In other words, there's an enormous literature.
8 And somehow one gets the impression that there's no
9 literature. So we get this document that talks about --
10 that it's not genotoxic that we get yesterday on E-mail,
11 which is another issue. But the fact of the matter is
12 they don't talk -- everything that I've just said, they
13 don't say one word about in their document. It's as
14 though it's selective reading of the literature.

15 Well, the fact of the matter is that it's very
16 likely that the toxicity of naphthalene occurs because of
17 naphthoquinones, and naphthoquinones produce reactive
18 oxygen species. They're genotoxic. They react with biol
19 groups, and so on and so forth. And we could spend hours
20 talking about this science.

21 So that to me the issue is -- should be obvious.
22 And the fact that it's not means that we're either not
23 looking at the literature properly or that people are
24 selectively looking at the literature, or whatever the
25 devil the reason. But I think that we can predict the

1 toxicity of naphthalene. I mean naphthalene produces
2 cataracts. You didn't put that on your slide, but we know
3 that. And so on and so forth. And those are
4 naphthoquinone metabolized.

5 So that the bottom line, as far as I'm concerned,
6 is I think it would be helpful if you had put a bit more
7 in your document, because I think the evidence is so
8 strong. But I think that the bottom line is that we need
9 to treat naphthalene very seriously given its -- one,
10 given the fact that it produced brain cancers, where in
11 the entire history of the NTP bioassay they had never seen
12 a control animal with the same tumors. So I don't know
13 how many control animals they looked at over the years,
14 but it must be 700,000 to 800,000. And they've never seen
15 that brain cancer.

16 I chair the NTP -- chaired -- past tense --
17 chaired the NTP Committee that reviewed naphthalene for
18 NTP. And our committee voted 9 to 0 to list it as
19 reasonably anticipated to be a carcinogen. So our
20 committee was made up of academics and others from around
21 the country. So that vote was clear. And the reason for
22 the vote was the uniqueness of the brain tumors that were
23 seen with naphthalene.

24 PANEL MEMBER BLANC: John, can you --

25 CHAIRPERSON FROINES: So I'm done. I just wanted

1 to -- I obviously have a big stake in naphthalene because
2 we do research on it. So I'm just full of -- I could talk
3 for hours. But I'll stop here. But the point is I think
4 we need to stop thinking -- we don't think of
5 benzo[a]pyrene as the carcinogen. We think of a whole
6 series of other kinds -- whether it be quinones or diol
7 epoxides or what have you. And we should treat
8 naphthalene the same way, I think.

9 Joe.

10 PANEL MEMBER LANDOLPH: Yeah, I agree with
11 everything you said. I think the other thing, you know,
12 you might want to incorporate into the discussion is -- as
13 you well pointed out, Dr. Brown, naphthalene has some
14 hematotoxicity. And I was sitting here thinking, you
15 know, that's exactly what Benzene has, and they both make
16 quinones and they both redox cycle.

17 And then as you go from Benzene to naphthalene up
18 to the higher congeners like benzopyrene, obviously you
19 make a quantum jump because those are able to, you know,
20 metabolize by P450 to diol epoxides and very efficiently
21 form DNA adducts, whereas Benzene and naphthalene don't.
22 Benzene's always been considered an outlier. But they act
23 more by virtue of redox cycling.

24 The higher polycyclics will also make quinones
25 which can redox cycle. So they can do both things.

1 Naphthalene and Benzene are missing the very strong DNA
2 adduction properties. But they're acting through
3 degeneration of these redox cycling quinones along the
4 ways John also mentioned.

5 PANEL MEMBER BLANC: So I guess --

6 CHAIRPERSON FROINES: And for ARB, we have a
7 method for measuring quinones -- for measuring quinones
8 across the Board in the air. And so one of the things
9 that ARB should consider is should you be measuring
10 quinones in your monitoring program, because they're out
11 there.

12 PANEL MEMBER BLANC: So, John, part of this
13 discussion in a way is reminiscent of our discussion of
14 Metam-Sodium and whether or not the OEHHA needed to
15 consider up front in that document Metam-Sodium and its
16 breakdown products, if you recall that discussion.

17 What I'm not -- I don't hear you going as far as
18 to say that this should be called -- that this document
19 should be on naphthalene and 1,4-naphthoquinone, are you?

20 CHAIRPERSON FROINES: Huh-uh.

21 PANEL MEMBER BLANC: So what you're saying rather
22 is that in appropriate sections, including the
23 introduction, there'll be more emphasis on the importance
24 of the quinone breakdown product and that it be made clear
25 that this occurs not only in -- as a metabolite and

1 biological systems, but as a photo-chemical or atmospheric
2 reaction by-product as well as a thermal breakdown product
3 in the combustion engines?

4 CHAIRPERSON FROINES: I'm basically reacting or
5 responding to this naphthalene is not genotoxic argument,
6 which we've gotten a number of comments including this
7 document that came in the mail yesterday. And it doesn't
8 address the main issues as far as I'm concerned. And so
9 I'm -- what I'm really saying is we need to I think have
10 in the document something that says -- that refers to some
11 of this literature that says, yes, there is more evidence.

12 Now, Joe's added some, because I hadn't seen that
13 slide before. Because he's took some of the
14 naphthoquinones and actually looked at some of the
15 genotoxicity data. And I don't know references those are
16 to.

17 So I think that we just could very easily and
18 briefly just strengthen the case by acknowledging that
19 there are pathways that have relevance.

20 SUPERVISING TOXICOLOGIST MARTY: We'd be happy to
21 do that.

22 STAFF TOXICOLOGIST BROWN: Sure. Easy.

23 CHAIRPERSON FROINES: But I didn't have any
24 comments on the risk assessment in a negative sense.

25 So I would make a motion that we approve --

1 PANEL MEMBER BLANC: Do you think the risk
2 assessment adequately takes into account by its design,
3 because of the animal data that it uses, the quinone
4 metabolite, or does it underestimate the risk by not
5 looking at pure quinone?

6 CHAIRPERSON FROINES: I think -- I think that the
7 uniqueness of those cancers is such that there's nothing
8 else you could do but use that. I would -- so, example,
9 if they had come in and wanted to use the mouse data, I
10 would have been unhappy with that. They didn't. They
11 came in -- I think that the tumor endpoint of consequence
12 is the rat tumor endpoint. And so, therefore, that's what
13 one should use for the risk assessment.

14 And, you know, as Joe and I both said, you know,
15 you've got this redox cycling and you've got electrophilic
16 activity which is more direct genotoxicity. And so that
17 would just muddy up the waters, I think, to try and look
18 at that. I don't think we really have the data to do it
19 anyway.

20 PANEL MEMBER BLANC: I have one small comment,
21 which I wouldn't even make except that it's generalizable
22 to other situations that you may be in when you're running
23 these reports, and I want to make sure that the
24 terminology is consistent.

25 There's a part where you're talking about the

1 non-cancer health effects. And you're dealing with
2 susceptibility to, you know, a med hemoglobin
3 degeneration, and you used the term "hypersensitive" to
4 this effect. And I would suggest that you don't use the
5 word "sensitive" as people may misinterpret that as
6 implying that -- susceptible is probably a better term.

7 CHAIRPERSON FROINES: By the way, there's also --
8 for Janette's and ARB's purposes, there's a fair
9 literature that's developing on using naphthalene as a
10 marker for jet fuel exposure. And I have those references
11 with me in case you're interested in taking a look at
12 them. Because they are -- clearly airports are something
13 that we need to spend some focus of attention at this
14 point. And there's -- I have -- there are quite a number
15 of articles that I piece together on the jet fuel issue.

16 So I make a motion that we accept the document,
17 recognizing that some small changes will be made.

18 Is that a --

19 PANEL MEMBER LANDOLPH: I'll second it.

20 CHAIRPERSON FROINES: Do we generally put -- Jim,
21 do we generally say recognizing or acknowledging that
22 small changes will be made in the resolution?

23 MR. BEHRMANN: Yes.

24 CHAIRPERSON FROINES: Or do we just --

25 PANEL MEMBER BLANC: Yeah, yeah, yeah.

1 CHAIRPERSON FROINES: Rather than just voting on
2 the document?

3 PANEL MEMBER BLANC: Yeah, yeah.

4 CHAIRPERSON FROINES: Okay. Further discussion?
5 All those in favor?

6 (Hands raised.)

7 CHAIRPERSON FROINES: Unanimous, 4 to 0.

8 So what time is it?

9 PANEL MEMBER BLANC: Time for lunch.

10 It's 12:20.

11 CHAIRPERSON FROINES: It's 12:20?

12 So we should take lunch and then come back and
13 start silica about what time?

14 1:30.

15 (Thereupon a lunch break was taken.)

16

17

18

19

20

21

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24

25

1 AFTERNOON SESSION

2 CHAIRPERSON FROINES: Why don't we get started.

3 Melanie, I think we'll just assume that Stan will
4 call in at some point. He probably has traffic problems
5 getting back.

6 You know, I know you people in northern
7 California have traffic problems, whereas we don't in
8 southern California.

9 SUPERVISING TOXICOLOGIST MARTY: Okay. The next
10 item for discussion is our chronic reference exposure
11 level for our respirable crystalline silica. This was
12 done under the Air Toxics Hot Spots Program.

13 So we'll be, in addition -- additional chronic
14 REL for risk assessments conducted under that program.

15 And Jim Collins and Andy Salmon will be giving
16 the presentation.

17 (Thereupon an overhead presentation was
18 Presented as follows.)

19 STAFF TOXICOLOGIST COLLINS: So, first of all I'd
20 like to go for the prior actions we've had on chronic
21 reference exposure levels.

22 The technical support document for determination
23 of non-cancer chronic reference exposure levels, an
24 initial draft was available for public comment October
25 1997. The second draft based on revisions of the first

1 was available in September 27th, 1999. We then presented
2 the guidelines in the first 22 chronic RELs to the panel.
3 And after the panel's endorsements the OEHHA Director
4 adopted the methodology and the chronic RELs on February
5 23rd, 2000.

6 In addition, there were three chronic RELs that
7 we had in existing TAC documents that were incorporated.
8 Those were acetaldehyde, perchloroethylene, and diesel
9 exhaust.

10 --o0o--

11 STAFF TOXICOLOGIST COLLINS: Subsequently, we
12 looked at several other batches of chemicals. We had
13 something called Batch 1B in which there were 16 RELs
14 adopted in April of 2000. Batch 2A had 22 RELs adopted in
15 January of 2001. Batch 2B, 12 RELs at the -- in December
16 2001. And then there were some individual chemicals,
17 carbon disulfide, phosphine, triethylamine, and fluoride,
18 that were adopted in 2002 and 3. So we have a total of 79
19 chronic reference exposure levels adopted so far.

20 --o0o--

21 STAFF TOXICOLOGIST COLLINS: The Hot Spots Act
22 was passed in 1987. And respirable crystalline silica was
23 listed as a Hot Spots chemical in 1988. The annual
24 emissions from stationary sources in California is
25 estimated to be approximately 3 million pounds. Some of

1 the sources and emissions are sand and gravel mining,
2 glassware manufacture, diatomaceous earth processing and
3 cal signing and other sources. A chronic REL was
4 requested by the ARB in 1998, and some air districts
5 requested the same thing in 2000. There's a large amount
6 of occupational data from human workplace exposure
7 available in peer review literature.

8 --o0o--

9 STAFF TOXICOLOGIST COLLINS: Is he on?

10 Several investigators are also concerned --

11 PANEL MEMBER GLANTZ: Hi. This is Stan.

12 STAFF TOXICOLOGIST COLLINS: Hi, Stan.

13 PANEL MEMBER GLANTZ: I can hardly hear you.

14 STAFF TOXICOLOGIST COLLINS: Okay. We're on the
15 fourth slide.

16 PANEL MEMBER GLANTZ: Okay. The fourth slide of
17 what?

18 STAFF TOXICOLOGIST COLLINS: Of the silica
19 presentation.

20 PANEL MEMBER GLANTZ: Okay.

21 STAFF TOXICOLOGIST COLLINS: It's the -- the
22 first bullet is listed as a Hot Spots chemical in 1988.

23 PANEL MEMBER GLANTZ: Okay.

24 STAFF TOXICOLOGIST COLLINS: Okay. The last
25 bullet: Several investigators are concerned that the risk

1 of silicosis at the workplace -- current workplace
2 standard of 50 micrograms per cubic meter --

3 PANEL MEMBER GLANTZ: You're kind of coming in
4 and out. I can't hear you.

5 PANEL MEMBER BLANC: Well, there's nothing we can
6 do about that, Stan.

7 STAFF TOXICOLOGIST COLLINS: How's that?

8 Okay. Next slide.

9 --o0o--

10 STAFF TOXICOLOGIST COLLINS: Now, although we're
11 going to dwell on silicosis as determined by x-ray and by
12 autopsy today, I'd also like to point out that the
13 American Thoracic Society stated that studies from many
14 different work environments suggested exposure to working
15 environments contaminated by silica at dust levels that
16 appear not to cause roentgenographically visible simple
17 silicosis can cause chronic air flow limitation and/or
18 mucous hypersecretion and/or pathologic emphysema.

19 --o0o--

20 STAFF TOXICOLOGIST COLLINS: Silicosis is an
21 irreversible, progressive fibrotic disease of the lungs
22 caused by inhaling crystalline silica. Some of the
23 cohorts of workers that have been studied are gold miners
24 in South Africa, gold miners in South Dakota, diatomaceous
25 earth workers in Lompoc, California, tin miners in China,

1 granite workers in Vermont, hard rock miners, Ontario,
2 Canada, and industrial sand workers in the United States.

3 --o0o--

4 STAFF TOXICOLOGIST COLLINS: For this REL we used
5 standard benchmark concentration method with the U.S.
6 EPA's BMDS software, which Joe Brown mentioned earlier.
7 The original method of doing RELs was the NOAEL/LOAEL
8 approach. But wherever data are available and we can use
9 a benchmark concentration, we attempt to do so.

10 As our key study we used a well-conducted epi
11 study of gold miners in South Africa, and we also
12 calculated RELs for several other cohorts which included
13 South Dakota gold miners, diatomaceous earth workers, and
14 Chinese tin miners.

15 --o0o--

16 STAFF TOXICOLOGIST COLLINS: The key study was a
17 study by Hnizdo and Sluis-Cremer, published in 1993. They
18 had a cohort of 2,235 white South African gold miners, who
19 had spent I believe a minimum of ten years doing
20 underground mining. And they found among that cohort 313
21 cases of silicosis as diagnosed by x-ray criteria.

22 The LOAEL for this cohort was approximately three
23 milligrams per cubic meter-years of cumulative dust
24 exposure. So a person exposed to one milligram per cubic
25 meter a year for three years would have that exposure, or

1 7-day-a-week exposure, which is 8.75. And then we applied
2 various uncertainty factors.

3 A LOAEL uncertainty factor is not needed in the
4 BMC approach. Since the people were exposed on the
5 average of 24 years, we did not need a subchronic
6 uncertainty factor. Since we looked at humans, we did not
7 need an interspecies uncertainty factor. But we did use
8 an uncertainty factor of three for intraspecies since,
9 among others, women, children, and elderly were generally
10 not found working in the mines. And the cumulative
11 uncertainty factor was three and, therefore, the chronic
12 REL based on this study was three micrograms per cubic
13 meter.

14 --o0o--

15 STAFF TOXICOLOGIST COLLINS: This is a fit of the
16 Probit model to the data. The P value was approximately
17 .99. Several other models adequately fit the data. We
18 took this one because the Probit model is a well used
19 model and the fit was quite good.

20 --o0o--

21 STAFF TOXICOLOGIST COLLINS: From some of the
22 other studies we also obtained estimates which were
23 similar to the original estimate. Steenland & Brown
24 studied the home state gold miners in South Dakota. They
25 found 170 cases of silicosis out of over 3,000 miners.

1 And using a BMD method, we ended up with an estimate of 4.

2 Hughes, et al., studied the diatomaceous earth
3 workers in California. There are 81 out of 1,800 miners
4 had silicosis.

5 The two values are based on an interpretation of
6 their data. If they're really looking at a NOAEL, which
7 they thought they were, the estimate of the BMD would be
8 ten micrograms per cubic meter. We believe that their
9 lowest score was probably a LOAEL, in which case he
10 thought that three micrograms per cubic meter would be a
11 more reliable benchmark for those.

12 Finally, Chen looked at 3,010 Chinese tin miners.
13 Over a thousand of these miners had radiographically --
14 were radiographic silicosis. And we ended up with an
15 estimate of six micrograms per cubic meter from that
16 cohort.

17 --o0o--

18 STAFF TOXICOLOGIST COLLINS: Some of the
19 strengths of this REL we believe are the availability of
20 several long-term studies of inhalation in workers at
21 varying exposure concentrations, with adequate
22 histopathological and radiologic analysis and adequate
23 follow-up; a dose response for silicosis in several
24 studies, which enabled us to do the benchmark
25 concentration; the observation of a NOAEL in some studies

1 including the key study; and the power of the key study to
2 detect a small effect, something on the order of a
3 one-percent incidence.

4 --o0o--

5 STAFF TOXICOLOGIST COLLINS: On the other hand,
6 the weaknesses. There was a limited follow-up in some of
7 the supporting studies. There was a general
8 underestimation of silicosis by radiography alone.
9 Generally a lot more cases are -- maybe 50 percent more
10 cases are found on autopsy. There's a lot of uncertainty
11 in the exposure estimation, especially in the early years
12 when the cohorts were exposed. And the variability and
13 the toxicity of various forms of crystalline silica.

14 How does this silica REL affect children? Is
15 there a potential for differential impacts? While there
16 is no direct evidence in the literature on differential
17 effects of silica in infants and children relative to
18 adults; however, there is evidence that particles are
19 more -- can be more deleterious to children's health than
20 adults. So we know -- specific interest information on
21 the silica particle, however, in general particles tend to
22 be more damages. OEHHA included an uncertainty factor of
23 3 to protect sensitive subpopulations, particularly
24 infants and children.

25 SUPERVISING TOXICOLOGIST MARTY: That's the end

1 of the presentation on actually what we did. And we have
2 several more slides on comments.

3 --o0o--

4 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

5 SALMON: Okay. I'll take over the presentation of the
6 comments here.

7 We received a series of comments. The authors of
8 these comments are listed here. Several of them are
9 consultants engaged by the American Chemistry Council's
10 Crystalline Silica Panel and there are some independent
11 commenters also.

12 --o0o--

13 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

14 SALMON: The first comment was that a chronic reference
15 exposure level for silica is not needed.

16 Our response to that is that we believe it is
17 needed based on the fact that we were asked to generate
18 one by the California Air Resources Board and the air
19 districts, and thinking that they're in good position to
20 know that one is useful for their purposes.

21 Bring up the next slide please.

22 --o0o--

23 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

24 SALMON: Part of the reason why they argued for the REL
25 being unnecessary was this second comment, that there is

1 no silicosis due to ambient silica.

2 We're not arguing that there is a problem with
3 occurrence of silicosis in the general population of
4 California due to exposure to ambient silica levels. And
5 one of the points we wanted to emphasize is that the
6 reference exposure level, which is above the ambient
7 levels generally found in California as we noted in the
8 report, the REL is defined as a level at which effects are
9 not expected to occur in the general population.

10 CHAIRPERSON FROINES: Andy, what -- I don't
11 remember. But what are the ambient levels that are
12 generally found in California?

13 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
14 SALMON: In the appendix to the report I think we list --
15 list levels up to about --

16 STAFF TOXICOLOGIST COLLINS: The very back of
17 this.

18 CHAIRPERSON FROINES: Pardon me?

19 SUPERVISING TOXICOLOGIST MARTY: We have some
20 data generated through the Air Resources Board for three
21 areas in California. It's on page 36 of the report, the
22 very last page. The means were two-tenths micrograms per
23 cubic meter, six-tenths, and 2.3 for those three areas.

24 The ranges went up to 3.46 in the highest area,
25 1.15 and 1.44 in the other two areas.

1 CHAIRPERSON FROINES: How were they measured?

2 SUPERVISING TOXICOLOGIST MARTY: This -- okay. I
3 may have to call ARB up here. But in talking with the
4 ARB, these were x-ray diffraction analyses of particulate
5 matter captured in typical PM10 samples. So it was not
6 PM10. It was the crystalline silica fraction of that
7 PM10.

8 STAFF TOXICOLOGIST COLLINS: We have the report,
9 if you'd like to see it.

10 CHAIRPERSON FROINES: We have what? I'm sorry.

11 STAFF TOXICOLOGIST COLLINS: I have the report,
12 if you'd like to see it, with us.

13 CHAIRPERSON FROINES: No, I just want to get an
14 order of magnitude.

15 So this is the database?

16 STAFF TOXICOLOGIST COLLINS: No.

17 CHAIRPERSON FROINES: This is it?

18 STAFF TOXICOLOGIST COLLINS: Oh, no, no. There's
19 a lot of other things. I mean, again, you know, you
20 have -- this is not an exposure analysis for California as
21 much as it is a risk assessment for silica. So there's
22 other data available, which is not presented in the
23 report.

24 SUPERVISING TOXICOLOGIST MARTY: There's one
25 study that was done in Lompoc that was actually

1 specifically done because of the concern of a diatomaceous
2 earth -- there's a mine close to the town and there's
3 actually a cal signing facility in the town. And there
4 was on the order of 30 or 40 samples taken, and only 3 of
5 them were above the limit of detection, which was about
6 half a microgram per cubic meter. So there's an
7 additional set of data. None of those data have been
8 published to my knowledge. But there aren't a whole lot
9 of samples that are -- or there hasn't been a lot of
10 monitoring for crystalline silica per se.

11 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
12 SALMON: There's a number of other values listed in the
13 appendix. The point is that most of these higher values
14 are basically near source measurements of some kind.
15 There are not a great many measurements of what you would
16 call general ambient backgrounds.

17 PANEL MEMBER BLANC: Well, I think you'll be
18 coming back to this, won't you, because one of the
19 recurring criticisms was that the REL is close to
20 background. So I assume that -- I think you should finish
21 your presentation of your responses. I want to see
22 whether that was one of the things that you're going to
23 address. And if not, we can go back to this issue.

24 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
25 SALMON: Well, our basic point is that we're not arguing

1 that the -- we're not arguing for a REL which is below the
2 general ambient background. It's above what we believe
3 the general ambient background to be in California.

4 And the other thing is the REL is not a standard
5 for application to general ambient backgrounds. It's a
6 standard to be applied in the assessment of emissions
7 which are modeled by a facility. So what the REL is
8 addressing would be an increment to whatever is present in
9 the background.

10 The way the Hot Spots Program works, normally you
11 would be running the emission inventory through some kind
12 of dispersion model and predicting what the additional
13 exposure resulting from the occurrence of that emission
14 would be at that science.

15 So we're not in any case arguing that we're
16 trying to -- you know, we're not advocating something
17 which would result in regulating the silica level back
18 down to background. And the assertion in some of the
19 comments to that effect is misguided.

20 CHAIRPERSON FROINES: I think we should go ahead
21 with the comments. I just want to say that it would be
22 interesting if somebody could tell us though what sort of
23 the South Coast or Bay Area Management Districts might do
24 with a number like this. Because there are -- local air
25 districts may view it as a regulatory value, whereas

1 that's not necessarily what you intended. So let's come
2 back to that.

3 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

4 SALMON: Yes, we can ask -- probably we should ask the Air
5 Board to address the regulatory implications.

6 Anyway, on the next comment. This comment is
7 that OEHHA should use the denominators from the exposure
8 duration classes identified in the life-table analysis
9 which was presented in the paper by Hnizdo and
10 Sluis-Cremer to define the ratio of cases to subjects at
11 risk in calculating the benchmark dose concentration.

12 --o0o--

13 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

14 SALMON: On the next slide I've got a table of the actual
15 numbers so you can see what this is about.

16 Basically what Hnizdo and Sluis-Cremer did was
17 they used a life-table analysis, which is a form of
18 time-dependent analysis, in order basically to provide,
19 firstly, a greater sensitivity to detection and
20 quantitation of the effect. And, secondly, to give some
21 idea of the time cost of development of the symptoms in
22 the cohort over the duration of the study.

23 And what we were doing by contrast was we were
24 basically using a cumulative incidence value, which was
25 the number of cases in each cumulative dose group which

1 had developed silicosis versus the total number of
2 individuals in that dose level group.

3 Now, what you can see here, the third column from
4 the left is from the life table. In effect what you have
5 is a moving snapshot of the cohort as the time progresses
6 through the study, and as you build up, exposure in
7 milligram per meter cubed years of cumulative exposure.
8 So all of the members of the cohort here had some exposure
9 in the range zero to two, in other words with a midpoint
10 of one milligram per meter cubed. Whereas, as you
11 increase the value of the midpoint of the cohort, so you
12 find fewer and fewer members of the cohort actually
13 reached that level of cumulative exposure.

14 So in fact only 197 members of the cohort
15 actually experienced between 10 and 12 milligram per meter
16 cubed years.

17 So in other words, this number at risk in the
18 life table is a sliding scale moving through the cohort.
19 Whereas, what we're doing is we're not doing the
20 time-dependent analysis at all. We're doing a simple
21 cumulative exposure at the end of the study basis for the
22 benchmark dose.

23 And one of the reasons for that is that we are
24 concerned about whole-life incidents. And the cumulative
25 incidents in this case lasted for an average of 24 years,

1 which we considered to be appropriate to form a basis for
2 judging the effects of a chronic exposure. But we did not
3 make any further adjustment to time beyond that.

4 In other words, we're not doing a time-dependent
5 analysis at all, mainly because we have absolutely no
6 information about how the lesion progresses or how the
7 appearance of the lesion would progress for time scales
8 outside of the duration of the study. And that to us was
9 a big uncertainty. We felt it didn't justify an attempt
10 to use a time-dependent analysis.

11 And I want to point out in looking at these
12 figures, that contrary to the implications in some aspects
13 of the comment we received, all of the members -- all
14 2,280 members of the cohort are represented in the groups
15 which we entered into our benchmark dose model. They're
16 in that model at the eventual cumulative dose level which
17 they achieved during the time course of the study. So if
18 you add up the numbers in the right hand, the fourth
19 column, which are the numbers at risk which we used, then
20 you get the total size of the whole cohort.

21 PANEL MEMBER BLANC: What about the 55 -- what
22 happened to the other 55 people, the difference between
23 144 and --

24 STAFF TOXICOLOGIST COLLINS: Oh, I'm sorry. I
25 couldn't get the last line on the slide. That's all.

1 They were all back in that --

2 PANEL MEMBER BLANC: There's one more row?

3 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

4 SALMON: There's an above -- there's a 13 and above
5 category.

6 PANEL MEMBER BLANC: Okay. And so -- it's okay
7 to take some time for questions, right? Because this was
8 a major point of back and forth.

9 If one did the other way around and was looking
10 at the 2218 entire cohort, you would be including within
11 the same group some people who had been exposed to, you
12 know, .05 of silica for 20 years and some people who had
13 been heavily exposed, but you're only counting first year
14 of their exposure and they couldn't possibly have
15 silicosis yet?

16 STAFF TOXICOLOGIST COLLINS: Ten years is a
17 minimum.

18 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

19 SALMON: Yeah, there's a ten-year minimum.

20 PANEL MEMBER BLANC: But in any event, there
21 could be people there who were 10 years and people who
22 were 30 years or so?

23 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

24 SALMON: Within each band of cumulative exposure there
25 could be people who racked up their cumulative exposure

1 during a period of 10 years and there would be people who
2 took up to 30 years to achieve that same cumulative
3 exposure.

4 But one of the conclusions of Hnizdo's analysis
5 was that the cumulative exposure was a respectable
6 exposure metric to use for assessing the appearance of
7 symptoms at least during the course of the study. So we
8 stayed with that exposure metric within the study.

9 PANEL MEMBER BLANC: And I know it's somewhat out
10 of order. But if Stan is still on the line --

11 PANEL MEMBER GLANTZ: Oh, yes.

12 PANEL MEMBER BLANC: I wonder since he was going
13 to address this topic, even though it's slightly out of
14 order, it would be kind of good to --

15 PANEL MEMBER GLANTZ: You know, you must be using
16 a different microphone, because I had no trouble with Andy
17 at all. So could you use his microphone, because you're
18 just dropping in and out.

19 PANEL MEMBER BLANC: Well, let me speak like
20 this, Stanley.

21 Can you make your comments on the life-table
22 analysis issue at this time?

23 PANEL MEMBER GLANTZ: Yes. Well, I've -- as I
24 mentioned this morning, I have looked at this and talked
25 it over with the staff. And I think what the OEHHA people

1 are doing makes sense. And I think that the alternative
2 analysis, which seems to be being proposed by the
3 commenters, doesn't make sense because I think it's kind
4 of a cross between what OEHHA did, which is a sort of dose
5 response and a life-table analysis. And as I understand
6 what the commenters are suggesting, they want -- if you
7 look at this -- is the slide still up there?

8 PANEL MEMBER BLANC: Yes.

9 PANEL MEMBER GLANTZ: Yeah, it seems to me
10 they're saying that you should be dividing the second
11 column -- or the third column by the second column. And
12 the third column is the sort of inverse cumulative density
13 function. And the first column is like an incidence rate.
14 And so that just doesn't make any sense to me at all.

15 So I support the kind of analysis that OEHHA did.
16 I think it's sensible and it's very straightforward.

17 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
18 SALMON: I want to make clear, we're not arguing that the
19 life-table analysis used by Hnizdo and Sluis-Cremer, and
20 advocated by Dr. Berry's comment -- we're not arguing
21 that's wrong as a life-table analysis for cohort study.
22 What we're saying is it's not what we chose to do and not
23 what we considered appropriate for the dose response
24 analysis that we made.

25 PANEL MEMBER GLANTZ: Right. And I think that

1 that's the point. I think that the -- what OEHHA is
2 trying to do here is get an estimate of the dose response
3 curve that accounts for the cumulative lifetime exposure
4 by using the data in the life table, but analyzing it a
5 little bit differently. And I think that that is a fairly
6 direct way to do it.

7 And I think if you go back to the life table,
8 you've got the problem of the magnitude of the dose and
9 also the temporal history, which isn't really being
10 considered if you do it the way the commenter suggested.

11 So, again, I think -- you know, the assumption
12 which is implicit in what OEHHA did is that the effect
13 should be proportional to the integrated dose -- the dose
14 integrated over time. But I don't think that's an
15 unrealistic assumption and it's something that's certainly
16 used in lots of other compounds.

17 PANEL MEMBER BLANC: Stan, Paul here again.
18 Would there be a problem also if -- even if one did the
19 other -- the other approach, that there would be an
20 absence of independence between the different ratios,
21 because you'd be counting -- for some things you'd be
22 counting the same people twice, wouldn't you? Or --

23 PANEL MEMBER GLANTZ: Well, I suppose -- I hadn't
24 thought about that. I suppose that's true. I mean I just
25 could not quite figure out why the approach that they were

1 advoc -- I could not get the approach they were advocating
2 to make sense to me. I mean maybe that's why.

3 PANEL MEMBER BLANC: Because I think one of the
4 problems that I sensed in the back and forth was that the
5 OEHHA staff were struggling with trying to put into words
6 the rationale in a simplistic enough way that any
7 reader -- that would be transparent to any reader. I mean
8 I think that --

9 PANEL MEMBER GLANTZ: Well, maybe what they
10 should say is what I -- which I don't think -- as I
11 recall, I don't remember reading in the report, is to
12 simply say that they are -- you know, they're including
13 time in the analysis in that they're looking at the
14 integrated dose over time.

15 And then they're looking at the number of people
16 who receive that temporally integrated dose and the number
17 of cases developed among people who received that
18 temporally integrated dose. And maybe making that
19 explicit will kind of resolve the controversy.

20 PANEL MEMBER BLANC: Well, I think also they need
21 to say that not only -- that the alternative is not an
22 alternative. The alternative is -- it's not something
23 we -- we chose to do it this way instead of this way is
24 the way it comes off. And really what you have to say is
25 were you to do it the other way, you would get the wrong

1 answer. And the reason you would get the wrong answer is
2 A, B and C. And I think part of that is in fact that
3 they're not independent -- you would be violating the
4 assumption of independence of observations.

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

6 SALMON: The way that they were suggesting we should do a
7 time-dependent analysis has a number of defects,
8 including --

9 PANEL MEMBER GLANTZ: Please stay close to the
10 microphone.

11 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

12 SALMON: Sorry.

13 The method which they were advocating we use in
14 order to do a time dependent dose response calculation has
15 a number of defects, one of which, as you point out, is
16 the lack of independence between the different values.
17 But the other issue which we -- were we to attempt to make
18 a time dependent analysis is the question of how we would
19 extrapolate from the study duration to a whole-life
20 exposure. So those are two issues which we didn't feel
21 that we had -- they're issues which in theory could have
22 been solved if we had access to the entire individual
23 data, as far as the independence is concerned.

24 If we had access to every single case
25 time-duration report, you know, for the raw study data,

1 one could address that methodologically. But one could
2 still not address the issue of how to extend out the
3 expected time cost to represent a whole-life exposure. So
4 we felt that the basic approach of using a time-dependent
5 analysis of incidence was inappropriate in this case.

6 But as you point out, we are using a
7 time-dependent exposure measure. But we elected not to
8 attempt to use a time-dependent incidence measure.

9 PANEL MEMBER HAMMOND: It would seem to me that
10 you would want -- what they're looking for is something
11 like person years at risk. And as you say, you need a lot
12 more data on them individually. And that's -- but that's
13 not what they proposed either. They're kind of in some
14 sort of crossways between --

15 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
16 SALMON: I think what they were trying to do was advocate
17 some simple fix that would accommodate their objective of
18 having us use the life-table data and also
19 coincidentally would -- in their perception I think it
20 would result in a higher reference exposure level.

21 However, I would like to point out that subject
22 to all these caveats and concerns and the fact we felt it
23 was inappropriate to use time-dependent analyses in this
24 case, nevertheless, if you make all these simplistic
25 assumptions and then adjust or attempt to adjust for the

1 study duration versus whole-life exposure, in fact you
2 come up with numbers from both the Hnizdo and Sluis-Cremer
3 data and also the Chen data which we analyzed as a
4 supporting study -- and Chen does also do a time-dependent
5 analysis -- if you make simplistic assumptions in order to
6 extend those to a whole-life value, you come up with
7 numbers which are not greatly different from the number
8 which we propose using our long time dependent analysis.

9 In other words, we're not pretending that we've
10 covered the temporal element here. But it doesn't in fact
11 make, you know, a huge difference with these data sets.

12 PANEL MEMBER GLANTZ: So would it -- I mean
13 that's actually a very important point. I mean would it
14 be useful to actually present those calculations as part
15 of the final response to comments?

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
17 SALMON: We can certainly do that. Yes, we --

18 PANEL MEMBER GLANTZ: Yeah, I think that would be
19 a good idea, because I think -- as I understood Kathi's
20 comment, what they were trying to do is sort of halfway in
21 between. And to do it properly you would have to do it
22 the way you were saying. And if that sort of analysis
23 leads you to essentially the same conclusion, I think that
24 would be worth having in the record.

25 I do think though one should, where at all

1 possible, strive toward the simpler approach. And I think
2 that the approach you have is pretty straightforward and
3 defensible.

4 PANEL MEMBER BLANC: Another way in which you
5 might be able to explain the pitfall of treating the data
6 in the way that the critics have proposed is through an
7 analogy -- by presenting an analogy.

8 For example, if you have a toxicologic study and
9 you had one -- and you have 50 rats that were exposed at
10 two parts per million for six months so that their
11 exposure was one part per million year and you'd had
12 another group of rats who were exposed at four parts per
13 million for six months so that their exposure was two
14 parts per million years. It would be as if saying -- and
15 you saw no tumors in either of those two groups, and then
16 you saw them in the higher group -- that you would say
17 that you had no tumors in a hundred mice at one part per
18 million year because, you know, the ones that had two
19 parts per million year certainly had one part per million
20 year. And then to then use that same 50 rats again, and
21 you couldn't do that, right?

22 So I mean -- that may not be the right analogy.
23 But I think that you may need to revert to some kind of
24 analogy to explain to the reader why the reasoning is
25 false.

1 PANEL MEMBER HAMMOND: That may be. But I think
2 the other way is -- more directly in terms of what you
3 have done, is to say you've taken each person, saw what
4 their cumulative exposure was and put them in the
5 appropriate bin, and that's how you did the calculation.
6 I think it's a straightforward way to say what you did do
7 as opposed to --

8 PANEL MEMBER GLANTZ: Yes, I agree with that.
9 And I think it would make the report clearer and more
10 defensible.

11 CHAIRPERSON FROINES: I agree with Paul though,
12 notwithstanding Kathi and Stan's doc. I think that the --
13 the approach that OEHHA's taken, which you want to be
14 particularly clarified, is relatively clear. I think
15 Paul's analogy is actually very useful about the
16 inappropriateness or the inadequacy of the alternative
17 view. I think that's the one that for me was the most
18 confusing. From a toxicologic standpoint, what you did
19 here was very clear. But the alternative was less clear
20 to me.

21 PANEL MEMBER HAMMOND: I think that's because it
22 doesn't really make sense.

23 CHAIRPERSON FROINES: What?

24 PANEL MEMBER HAMMOND: I think it's because the
25 alternative presented doesn't really make sense because

1 it's part way towards something else.

2 CHAIRPERSON FROINES: Well, it may be me and it
3 may be them, but I don't know which.

4 PANEL MEMBER HAMMOND: But I think that it's a --
5 actually since I'm new to this process, you can correct me
6 on this -- but I'm thinking that in the document that's
7 the statement you want to be clear and say this is what it
8 is. And in response to the comments, that's where you can
9 go through these other possibilities and what they mean.
10 But I think if you try to defend all of the -- it would be
11 confusing --

12 PANEL MEMBER BLANC: Yeah, yeah, I agree. I mean
13 what I -- for the analogy piece I would say that that
14 would be something you might do in a response. But for
15 the -- in the document you want to be clearer. I think it
16 is clear to say that in this method of analysis each
17 person appears on the analysis only once, whereas
18 alternative analyses would have people appear more than
19 once in the same analysis. I mean I think that you should
20 say in the main body of the --

21 CHAIRPERSON FROINES: I think that -- yeah, I
22 think that we're agreed, that those comments should be in
23 the response to comments, because you don't want to add a
24 lot of discussion to your basic document. It makes it
25 messier.

1 PANEL MEMBER BLANC: But it could have been
2 clearer in the basic document than it was.

3 PANEL MEMBER HAMMOND: I think the basic -- yeah,
4 I think the basic document does need to say
5 straightforward that each person is put into bin that
6 they -- not that colloquial.

7 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
8 SALMON: We can clarify that certainly. And we can add to
9 the response to comments as well.

10 I think we mentioned calculation on the Chen data
11 as part of our response to comment. But we can expand on
12 that a bit if you want to see that.

13 PANEL MEMBER BLANC: Well, you know, that
14 actually -- by the way, the -- I agree with Stan that
15 putting a couple of lines actually in the body of the
16 report that one does as an alternative, a life-table
17 analysis that assumes people go on to live X number of
18 years, you know, although not the basis of this evaluation
19 as a -- you know, as a comparison yields the following.
20 And you've done that in other documents before. And I
21 think that that in the body of the text is often
22 illuminating in the same way that using multiple studies
23 and showing what they yield is appropriate to the body.

24 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
25 SALMON: Okay. Shall I get on to the next comment then?

1 subsequently.

2 What we saw was it was actually quite a
3 considerable range of estimates, with the estimate from
4 Kielblock, which is a very large and fairly recent study,
5 covering a number of different mines. And so the
6 Kielblock report is extensive and it's based on very
7 extensive data. But that produces a low estimate of 15 --

8 CHAIRPERSON FROINES: What were the location of
9 those mines?

10 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
11 SALMON: It's all in South Africa. All these are -- yes,
12 these are all South African mine estimates. And they're
13 all similar sorts of mines.

14 Basically we have a range of estimates, from the
15 low end of 15 percent with Kielblock, to the high end of
16 Gibbs and Du Toit at 54 percent. So we felt that rather
17 than relying on any one basis for estimating the
18 percentage of silica, it would be better to look at the
19 overall database, and not take only the highest values
20 suggested by the commenter nor, conversely, should we take
21 the lowest value from Kielblock. So we chose a number
22 somewhere in the middle, which coincidentally is 30
23 percent, which is what we had to begin with. But we're
24 now basing that 30 percent not merely on the individual
25 report of Hnizdo, but on the full range of data that was

1 available for our consideration.

2 PANEL MEMBER HAMMOND: John, do you want this --
3 this is so complex, there's so many things. Should we ask
4 questions at this point?

5 Okay. Are you done with that?

6 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

7 SALMON: Yes.

8 PANEL MEMBER HAMMOND: Okay. I'm concerned
9 actually about this.

10 Could you tell me what is the median year that
11 people started work in the study of these workers?

12 STAFF TOXICOLOGIST COLLINS: I think it was 1938.

13 PANEL MEMBER HAMMOND: 1938 is the median year?

14 And is there any reason that people think that
15 the percent silica would have changed through the years?
16 Is there any evidence that there's like going through
17 different scenes or --

18 STAFF TOXICOLOGIST COLLINS: Oh, I would guess
19 the more recent determination could have been more
20 accurate.

21 PANEL MEMBER HAMMOND: That was kind of my point,
22 whether this is an analytical issue or whether it's a true
23 temporal change in composition.

24 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

25 SALMON: I think it's fair to say that the dust levels

1 have probably been reduced. But I don't think there's
2 any --

3 PANEL MEMBER HAMMOND: No, but the composition --

4 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

5 SALMON: I'm not aware of any data suggesting that the
6 composition has changed. And the geological formations
7 which they're working through are basically similar
8 throughout the period. They're basically --

9 CHAIRPERSON FROINES: But it's not quite that
10 simple, because the tools that one uses will generate
11 different percentages of silica. It's not simply what
12 you're actually mining, but it's actually what ends up
13 being earth wise to --

14 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

15 SALMON: There may be differences. But we're not aware of
16 any data either to say they are or say what they would be.

17 PANEL MEMBER HAMMOND: I guess -- and the years
18 that you've given are the years for which the samples were
19 taken that yielded the percentage that we've listed; is
20 that correct?

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: Samples --

23 PANEL MEMBER HAMMOND: For instance, Rendall, '56
24 to '72.

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: Yes.

2 PANEL MEMBER HAMMOND: But that 22 percent
3 represents samples collected in those years, '56 to '72;
4 is that correct? Am I understanding that correctly?

5 SUPERVISING TOXICOLOGIST MARTY: Yes.

6 PANEL MEMBER HAMMOND: That Rendall, '56 to '72.

7 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

8 SALMON: Yes.

9 PANEL MEMBER HAMMOND: Okay. Because what I'm
10 struck by is that -- I mean is -- in the data in the top
11 line, is that including the data -- Rendall's data? The
12 data points that Rendall used, are those also included in
13 the Hnizdo --

14 STAFF TOXICOLOGIST COLLINS: I don't think so.

15 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

16 SALMON: No. It is a separate -- it's a separate
17 determination. Hnizdo refers to Rendall's supporting
18 data.

19 PANEL MEMBER HAMMOND: Okay. Because I'm quite
20 struck -- if we leave out the top two lines, you know, I
21 mean that it looks to me as though most of the data is
22 actually lower and that in fact --

23 STAFF TOXICOLOGIST COLLINS: In the cohort the
24 last -- exposure in the dust was 1971. The first year was
25 about 1940.

1 PANEL MEMBER HAMMOND: Right. And I think that
2 the methods that were used to do -- examine the methods
3 were used for the analysis of the crystalline silica?

4 STAFF TOXICOLOGIST COLLINS: Not in an extent,
5 no.

6 PANEL MEMBER HAMMOND: Because I would be quite
7 concerned about, you know -- I would think that the
8 analytical methods would become more accurate over time.
9 And notwithstanding John's concern, which I think is quite
10 an issue as well, but if I look at that data, if I were to
11 make an assumption, I think I would be saying that
12 probably the composition is 20 percent silica,
13 something -- I mean it just -- now, I haven't looked at
14 the whole data and all those papers.

15 But because someone puts another number out and
16 then -- you know, that's twice as high as the number
17 you've had and then you've got all -- all your other data
18 were lower -- and all the reported data are lower, now
19 that you can average them and then come out with the same
20 number, well, I'm not sure that's really the same thing.
21 I think the truth may lie by looking deeply at what's
22 there. And it may be that the dust in the past was
23 actually only 20 percent silica. And you may actually be
24 overestimating the pass rather than underestimating the
25 pass --

1 CHAIRPERSON FROINES: Well, one of the questions
2 I have is when -- what's the timeframe for analysis of the
3 samples? In other words, what methods are -- basically
4 I'm asking what methods are being used to do the analyses?
5 Because if you're analyzing -- if you've got data from
6 the -- you know, the people analyzed with infrared way
7 back when as opposed to x-ray a fraction, you're going to
8 get very different numbers potentially.

9 PANEL MEMBER HAMMOND: Well, that's what I'm
10 asking. I think we actually need to look -- one would
11 need to look at the methods used and take that into
12 account in terms of how you weight it and look at that.

13 PANEL MEMBER BLANC: Well, isn't the -- this is a
14 related comment. But the big argument that the criticism
15 used was that the Hnizdo and Sluis-Cremer analysis was not
16 acid washed and that the Gibbs and Du Toit estimate was on
17 acid wash specimens, but what you're a little bit vague in
18 in your response is whether the other three analyses were
19 acid washed. So that at least on the four estimates it's
20 comparable methods.

21 PANEL MEMBER HAMMOND: Except that also my
22 understanding when you acid wash is that the acid wash is
23 taking away organic material. So you're taking -- you're
24 actually taking away from your denominator.

25 PANEL MEMBER BLANC: Well, I know. But I just

1 wonder if they're comparable to start with. We need to
2 talk about, you know, the interpretation of that.

3 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
4 SALMON: I think most of these determinations are using
5 the -- this method -- this gravimetric method, which I
6 think involves both cal signing the dust to remove organic
7 material and then acid washing it to remove soluble
8 minerals.

9 PANEL MEMBER BLANC: Well, see, that's part of
10 the problem. I think you have to be more confident in
11 your response. You institutionally. I think that the
12 report needs to be -- I think in one hand, in the body of
13 the report the reader is never really prepared for this
14 issue when it later comes up in discussing specific data.

15 There's an allusion to how crystalline silica is
16 measured or not measured, but it's not discussed in
17 sufficient detail in a neutral way early on: Here are the
18 major methods that are used; here are their strengths and
19 weaknesses; and in the United States x-ray diffraction is
20 used and these other places it's just by weight, inferring
21 that the only thing left after, you know, five different
22 steps must be silica because anything else would have been
23 eaten away or dissolved or whatever.

24 And, therefore, you know, a test done by this
25 method is, you know -- and if you do that, other data has

1 shown that it is 95 percent homologous with data that will
2 be used in the United States based on x-ray diffraction.

3 Because, after all, if later on it's not this
4 method that's used here for the silica quantification and
5 if there's some, you know, error or difference
6 systematically, you need to know that because you're
7 making all of your inferences based on this study. So
8 that's one thing I would suggest.

9 The other thing is -- let's assume a scenario
10 where Gibbs and Rendall and the second Hnizdo and the
11 Kielblock all did use exactly the same methods and you
12 have those papers and you know the end. Then what I would
13 suggest is rather than making the argument which is "Well,
14 we don't really know so we're going to use the first value
15 of 30 percent," in which unfortunately you've been boxed
16 into a corner by Dr. Hnizdo because her responses are so
17 inadequate and you've then invoked these inadequate
18 responses.

19 And then what you do is you say, "Well, we're
20 going to use her 30-percent data anyway because everything
21 else comes out near to it." Why not instead of that -- if
22 these are all using similar methods and you believe that
23 the method is valid, why not take the ends, calculate a
24 pooled percentage and use that. And even if it comes out
25 to be 28.9 percent or 31.2 percent, you'll be on such

1 stronger ground rather than trying to defend this position
2 which sounds so indefensible, you know, back and forth and
3 back yourself in a corner.

4 PANEL MEMBER LANDOLPH: Yeah, I had the same
5 feeling, because I was reading through this. That's
6 obviously an issue that comes up. I just averaged the
7 most -- 26 percent if you average all those values.

8 PANEL MEMBER BLANC: Assuming it's the same end.
9 But it may not -- it's a weighted -- you need a
10 weighted --

11 PANEL MEMBER HAMMOND: Well, and not only that it
12 has to be -- make sure it's the same methods, the
13 analytical methods. You have to check all that out, you
14 know.

15 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
16 SALMON: Yes.

17 PANEL MEMBER HAMMOND: And if they're different
18 methods, you need to look at what are the biases of the
19 method? Is it known to be high or low as you look at
20 that?

21 PANEL MEMBER BLANC: And the other thing is -- am
22 I assuming that you actually have in hand Dr. Rendall's
23 doctoral thesis?

24 STAFF TOXICOLOGIST COLLINS: I don't. Hnizdo --
25 we have Kielblock's, we have Gibbs and Du Toit.

1 PANEL MEMBER BLANC: So you need to get the
2 thesis and you need to cite the thesis. You
3 inappropriately say this is an unpublished document. But
4 a doctoral thesis is the equivalent of a published, you
5 know, thing in a way. It has a citation. I looked on
6 World Cat and couldn't find it. So the South African
7 libraries may not be in the system. I looked in, but --
8 you know, if somebody had a doctoral thesis from Columbia,
9 I'd be able to cite it.

10 So you need it. It's critical enough to what
11 you're arguing. It makes you seem sloppier than you are.
12 It just doesn't -- you don't do yourselves enough credit
13 when you do something like that. So --

14 PANEL MEMBER LANDOLPH: They have any error bars
15 presented in any of those publications? Those would be
16 useful to present too since obviously you're being
17 harassed to find that number. Although the methods may be
18 so different, it may overwhelm the error bars, but it
19 would be useful to have it.

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
21 SALMON: Yeah, I think -- well, if we were to do a
22 weighted mean, then we would be able to present those data
23 as well. So clearly that's something we should look into.

24 CHAIRPERSON FROINES: Well, what's your sense of
25 those studies in terms of the methodologies used at this

1 point?

2 SUPERVISING TOXICOLOGIST MARTY: I think we need
3 to look into it more to really get a better sense.

4 PANEL MEMBER GLANTZ: Would you speak closer to
5 the microphone.

6 SUPERVISING TOXICOLOGIST MARTY: We need to look
7 into it more to get a better sense of the comparability of
8 the methods that were used as well as the sampling size,
9 how many samples did they actually take, and so on, and
10 use that information to do a weighted mean.

11 I'm not sure it will be too much different than
12 30 percent, but it would certainly strengthen the
13 argument.

14 PANEL MEMBER HAMMOND: But it might be 20
15 percent.

16 PANEL MEMBER BLANC: And also you should -- and
17 you should not include the Hnizdo first-line data in that
18 because you already know that those were -- or you have
19 reason to believe that those were not acid washed. And
20 that's their whole argument. So then don't use them. Use
21 these other ones and average them if that's what it takes,
22 if they're all -- assuming that they're all comparable.

23 PANEL MEMBER LANDOLPH: I like the fact that your
24 numbers from the four studies actually came out pretty
25 close. They're not dramatically off for the REL. There

1 was very good agreement there.

2 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

3 SALMON: Okay. The next comment is the -- well, the
4 comment was that the studies which we cite as supporting
5 studies are not sufficiently reliable to be used.

6 We disagree. We recognize that the studies have
7 limitations, particularly things like length of follow-up,
8 which would result in under-estimation of the effect
9 because of the progressive onset of disease after
10 association of exposure.

11 But nevertheless we feel that in spite of these
12 imperfections it is useful to include them as supporting
13 studies in the narrative. But obviously we give them less
14 credence than we give to the Hnizdo and Sluis-Cremer study
15 for that reason.

16 --o0o--

17 CHAIRPERSON FROINES: Sorry. Would you repeat
18 the last sentence you said again. Somehow I didn't
19 connect with a --

20 PANEL MEMBER GLANTZ: I can't hear again.

21 STAFF TOXICOLOGIST COLLINS: Last sentence.

22 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

23 SALMON: Okay. I'll repeat what I -- what I said
24 basically is that we recognize that the supporting studies
25 have limitations. But we considered it was appropriate to

1 include them in the report as supporting studies. And
2 that we obviously give them less weight in determining
3 what we should recommend as a REL than we give to what we
4 consider the more reliable study, which is that by Hnizdo
5 and Sluis-Cremer.

6 So we're not discounting them, but we're not
7 weighting them as heavily in our overall consideration.
8 We're just looking at them for supporting evidence rather
9 than as a primary source of a recommended number. Okay.

10 PANEL MEMBER BLANC: Have you gone back to --
11 this is sort of a long shot. But when these publications
12 came out in the journals in which they came out, were any
13 of them accompanied by editorials? Especially the
14 Steenland one.

15 STAFF TOXICOLOGIST COLLINS: I don't recall. I
16 can go back and check.

17 PANEL MEMBER BLANC: I think you should double
18 check. Because if they were, I think you might cite the
19 editorial comments that were made at the time.

20 CHAIRPERSON FROINES: Well, we know there was an
21 editorial on silicosis in the American Journal of
22 Industrial Medicine. I can't remember, was it Ian Greaves
23 or Harvey Checkoway wrote it?

24 STAFF TOXICOLOGIST COLLINS: Or was it Cocce?

25 CHAIRPERSON FROINES: It was not very long ago.

1 STAFF TOXICOLOGIST COLLINS: There was I think
2 Cocce -- somebody from Italy wrote on a -- C-o-c-c-e.

3 CHAIRPERSON FROINES: No. But Harvey or Ian
4 wrote editorials on this issue in the American Journal of
5 Industrial Medicine in the last three or four years.

6 STAFF TOXICOLOGIST COLLINS: You mean "Greaves on
7 Not So Simple Silicosis," that article?

8 CHAIRPERSON FROINES: No, I'm talking about an
9 editorial.

10 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
11 SALMON: Well, we can try and track -- we'll try and track
12 those down.

13 CHAIRPERSON FROINES: But they specifically
14 talked about the dose response relationship to Silica.

15 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
16 SALMON: I know -- I'm pretty sure Checkoway has written
17 several things on that topic. I seem to remember seeing
18 both editorials and published papers. We'll look for
19 those.

20 CHAIRPERSON FROINES: I have a little trouble
21 with what you said. Because when you say you don't give
22 it as much weight or you weight it -- that sounds like
23 something quantitative, when I think you actually mean it
24 in a very qualitative descriptive sense.

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: Yes.

2 CHAIRPERSON FROINES: And so that in part one
3 would like to know what the limitations were that made
4 it -- because some of those studies that you quoted were
5 actually quite good studies. And so when you say that
6 they are -- they're problematic, or imply that, I think
7 that even -- you know, Ken Rosenman studied from me a few
8 years ago and so on and so forth.

9 A lot of -- there was some very good work on
10 this. So it's not clear to me that -- I thought that
11 using other studies was a very good device actually, very
12 useful. And so what I'm worried about is creating a
13 transcript where you're saying that they had such
14 limitations that you gave them less weight. And I'm not
15 sure you really mean that.

16 PANEL MEMBER HAMMOND: I think actually you did
17 say it, but I think it doesn't come across as strongly,
18 that the important thing is the limitations of the studies
19 you identify are limitations such that they would
20 underestimate the effect. You say that. I think that's a
21 very important point.

22 I mean it shouldn't be buried in there, you know,
23 so that -- in fact, anything, you know, the effect is
24 stronger than what you've got. And even with that you get
25 to the same number.

1 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

2 SALMON: Yes, I think it's true to say that the
3 limitations we're talking about -- and, Jim, I don't know
4 whether you can back me up on this. But it's my
5 impression that among the specific limitations which we're
6 concerned with for I think both the Steenland and the Chen
7 study is length of -- is length of follow-up, which
8 specifically will underestimate -- we're not saying that
9 they're poorly executed or not good studies. We're saying
10 that they would produce a less good number for our
11 purpose.

12 PANEL MEMBER HAMMOND: But, no, no, don't say it
13 that way. I would say that they end up -- they're going
14 to under-count the number of cases of silicosis because
15 they don't continue to follow to death.

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

17 SALMON: Yes, exactly.

18 STAFF TOXICOLOGIST COLLINS: And that's certainly
19 the case of the gold miners in Ontario.

20 PANEL MEMBER HAMMOND: Right. No, I know. But
21 the point is that clearly it's a direction and it's a
22 direction that underestimates them.

23 STAFF TOXICOLOGIST COLLINS: Um-hmm.

24 CHAIRPERSON FROINES: Go ahead.

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: Okay. The next comment suggested that we had
2 some incorrect values in some other parts of the document
3 where we cite NOAELs and LOAELs. There is one case where
4 we had quoted the mean of an exposure band rather than the
5 upper limit when sizing a NOAEL in the Hnizdo and
6 Sluis-Cremer study. So we have corrected that. But that
7 doesn't have any bearing on the recommendation for chronic
8 RELs since we weren't using the NOAEL approach to derive
9 that.

10 The other NOAELs and LOAELs which we were accused
11 of having got wrong were those which we simply -- we were
12 citing another author. And we consider that we're correct
13 in citing those as given by those authors.

14 --o0o--

15 SUPERVISING TOXICOLOGIST MARTY: We have -- the
16 last important comment that we wanted to discuss, which is
17 coming up -- next slide, Jim.

18 Thank you.

19 --o0o--

20 STAFF TOXICOLOGIST COLLINS: We just wanted to
21 say that in particular we want panel input on to this one.
22 It gave us heartburn, and we thought that the commenters
23 had valid points that were in our estimation difficult for
24 us to deal with.

25 PANEL MEMBER HAMMOND: I think -- Oh, you should

1 go ahead -- sorry -- first.

2 CHAIRPERSON FROINES: Before you go to that, can
3 I go back to the issue of the percent silica. The more I
4 think about it, the more I think that the 54 percent is an
5 overestimate based on the notion of acid washing. And
6 that in some respects this notion of -- we had everything
7 that went from 15 to 54 percent and, therefore, we took
8 30.

9 I think -- I mean you do address the hydrochloric
10 acid issue. But I do think it's important for us to
11 recognize that acid washing is not without its impact and
12 we need to be quite serious about that, because we may be
13 overestimating the percent silica as a result of that.

14 Don't you think, Kathi?

15 PANEL MEMBER HAMMOND: I think that's what I
16 tried to say earlier. I was trying to say exactly that
17 earlier. But I think that one has to look at every one of
18 those studies, look exactly how they did it, and think to
19 yourself -- you know, get an analytical chemist to look at
20 it and say what is the effect, how close is it? If
21 there's an error, is this over or underestimating each
22 study, you know. And I would actually make a table that
23 ends up, you know, comparing these that tells you what the
24 methods are.

25 CHAIRPERSON FROINES: I think a little more work

1 needs --

2 PANEL MEMBER HAMMOND: And I think laying it out
3 carefully. And also to the degree one can know the error
4 in which the samples were collected as well as the method
5 that was used for the analysis, and if the bias is high or
6 low in the percent silica. You know, and I think putting
7 that all out there and then systematically looking at it.

8 And, you know, what it comes -- I don't think
9 taking an average of several numbers, six of which are
10 very good and two of which are terrible, is a good idea.
11 You know, I think you evaluate them. And if six of them
12 are good, you look at those and may take the average of
13 those, unless you see a temporal trend.

14 CHAIRPERSON FROINES: Paul's out of the room and
15 I want to go out of the room. And so can we take a
16 five-minute break so that we have a whole panel here for
17 this discussion. Because obviously --

18 PANEL MEMBER GLANTZ: Yeah, this is Stan. I'm
19 going to have to leave -- I mean I'm happy to take a
20 five-minute break, too, but I'm going to have to leave at
21 3:00.

22 (Thereupon a recess was taken.)

23 CHAIRPERSON FROINES: Okay. Let's get going.
24 Melanie, go ahead please.

25 SUPERVISING TOXICOLOGIST MARTY: Okay. The next

1 slide deals with the size fraction that the reference
2 exposure level should be applied to in a risk assessment
3 scenario. In the draft that went out for public review
4 and also went to the panel, we simply put crystalline
5 silica respirable, meaning PM10 fraction. That
6 encompasses a larger size fraction than was actually
7 measured in the epidemiological studies where they -- the
8 measurement method essentially used a PR4 sampling device.

9 So the criticism is that you're counting too much
10 silica if you're relying on the silica fraction, that is,
11 PM10; and that, therefore, you are overestimating the
12 health risk.

13 We were trying to figure out how best to handle
14 that, because in fact that's probably right. We know that
15 for regulatory purposes in California we define respirable
16 as PM10. The occupational community typically views it as
17 what is measured in their devices where PM4 is the median
18 size captured. And then we also in California look at
19 PM2.5.

20 So we thought we'd put in PM10 just to get the
21 reactions from those folks who know a lot more about this
22 on the panel in terms of how much they think that might
23 overestimate the total silica exposure. And some of the
24 thinking is the ideas for silicosis, that you have to
25 actually get all the way into the alveolus. That may not

1 be true for some of the other effects of crystalline
2 silica. COPD, for example, where you can reach the
3 bronchioles and the smaller airways and have some toxicity
4 in those airways.

5 So that's one of the considerations that you
6 really should be looking at, just the tinier fraction of
7 PM10. We don't have data on the size distribution of the
8 particles in any of the epi studies. We don't have data
9 on the size distribution of the particles that will be
10 emitted from some of the facilities of concern in
11 California. So it's hard to have any information that
12 would allow for a correction factor to be applied in a
13 risk assessment.

14 And most of the measurements we have, at least of
15 background levels, are, as I said earlier, based on PM10
16 and looking at the fraction of PM10 that is actually
17 crystalline silica.

18 So with that I will turn it over to the panel.

19 CHAIRPERSON FROINES: Kathi.

20 PANEL MEMBER HAMMOND: This is the area I think
21 that I'm most concerned with in the document. Let's see,
22 first of all -- well, I don't think one should refer to
23 the occupational measurements as PM4. I think that -- and
24 I think that it's not true that it's -- the mass median
25 diameter is four microns. That's an incorrect statement

1 as well. What it is is that 50 percent of four micron
2 particles will pass the size selector, which is a
3 different statement. A hundred percent of the particles
4 could be one micron in size and it would still be
5 respirable. So it doesn't tell you the size distribution
6 of the particles. It tells you the distribution -- the
7 percentage of each size that's allowed to pass.

8 The occupational respirable samplers are designed
9 to simulate what penetrates to the deep lung, to the
10 alveolar, and, therefore, are most relevant for silicosis,
11 and I think that's where they were first developed in
12 that. And it's important to be aware of that so that they
13 are, as you have said in the document, a health-based
14 collection method. It's a broader size cut. Whereas as
15 the PM2.5 and PM10 attempt to be a vertical size cut. If
16 you could do it absolutely perfectly, it would be
17 excluding everything greater than PM10 and including
18 everything less than PM -- no -- 10 microns in size.

19 So I think it's important to, you know, keep
20 aware -- keep the terms straight. So it is confusing.

21 But the term "respirable particles" is the
22 internationally recognized term in general for this
23 distribution that relates to what penetrates.

24 Given that in different settings there are
25 different distributions of particle size, you really can't

1 take -- there's no place to take from a PM10 to the
2 respirable particles, as you well recognize. But I'm
3 afraid that adopting a number that comes from a PM -- from
4 the respirable particle data literature and the
5 epidemiology and just saying PM10, well, it would
6 certainly be protected. But I think there is a real risk
7 that you'll be including many larger particle sizes.

8 And just to say, when I served on the TLV
9 Committee many years ago, we were very much grappling with
10 this issue of how we take data that was collected, is
11 slightly different, but the data were collected as -- was
12 nominally total particulate, but it was probably closer to
13 a -- something like a PM20 but what was collected on a
14 total particulate, and then applying it to if we were to
15 go to the inspirable sampling methods, you know, are the
16 inhalable sampling methods.

17 So there are a lot of issues going on here. And
18 other people are grappling with of how to go -- data
19 collected epidemiologically in one size fraction, how do
20 we apply it to another size fraction that's more
21 appropriate for sampling. It's a big issue.

22 One of the ways to deal with that is simply --
23 simply -- it's not simple -- but to go out and collect a
24 lot of data side by side. So, for instance, collecting
25 PM2.5, PM10, and respirable samples side by side in a

1 variety of locations and seeing what those -- how those
2 relate would be one very important piece of getting
3 information, and understanding what's going on.

4 And my understanding is that to the degree we
5 have information about silica, not necessarily crystalline
6 silica, but it may well parallel that, that silica in the
7 coarse fraction, in the PM2.5 to PM10 range, is in fact
8 has much more silica than PM2.5 does. So we know there's
9 a difference there.

10 And the respirable particles are, you know, kind
11 of quasi, a little more like the PM2.5, although there are
12 some problems within that.

13 So I think you really need to -- one needs to get
14 data, if at all possible, to do some side-by-side
15 sampling. Or, alternatively, to say that this REL applies
16 to respirable particles as defined by the occupation
17 literature, and not to try to impose the PM10 and PM2.5
18 standards, because in fact that's the most biologically
19 relevant size cut in the first place. So maybe bending
20 things around to other ways.

21 And there really is no reason that -- those
22 samplers can be designed. There's no reason you can't
23 have those. They do -- you can do respirable size sample.
24 But you do run into sensitivity issues, but you can adjust
25 those. People know how to set those -- design those

1 samplers to do the right size cut at different flow rates.
2 So you can actually do that. But it's not simple. I mean
3 there's work that would have to be done. But I think if
4 it's worthwhile setting a REL, it's worth getting it
5 right.

6 CHAIRPERSON FROINES: Are you suggesting size
7 distribution studies or are you suggesting --

8 CHAIRPERSON FROINES: I can't hear.

9 CHAIRPERSON FROINES: I'm not a hundred percent
10 clear on what Kathi just recommended in terms of this --

11 PANEL MEMBER HAMMOND: I was recommending
12 specifically -- I mean one could do size distribution
13 studies. That would be a way to do it.

14 I was suggesting -- since PM10 and PM2.5 are the
15 samplers that are out there and readily available to ARB,
16 so those are what are seen as the two choices that you
17 have as I understand it, that one would want to sample
18 with those two and with the true respirable by the
19 occupational definition samples; all three of those side
20 by side, in a variety of locations, to see how they relate
21 to each other.

22 Now, it's actually true that if you did -- if you
23 did a full-size distribution, you would be able to
24 calculate that.

25 CHAIRPERSON FROINES: But I think that that's

1 really not feasible, because, yes, you can go out and make
2 measurements, but those -- and one can do then a
3 statistical analysis on the data that you have and say,
4 "We can live with that"; but as we all know, the size
5 distributions can change dramatically and so it throws
6 that data into question about --

7 PANEL MEMBER HAMMOND: My primary -- you know, my
8 primary recommendation is not that. My primary
9 recommendation would be to say that the REL should be
10 applicable to respirable particles as defined occupational
11 because what's the epidemiology data is and it's the size
12 distribution that's appropriate for the health outcome
13 under consideration. Because the other ones that you've
14 mentioned, COPD, are not part of the -- they're not the
15 basis of the REL.

16 CHAIRPERSON FROINES: Paul.

17 PANEL MEMBER GLANTZ: This is Stan. I'm going to
18 have to sign off now. But I have said the main things I
19 had to say on this issue.

20 CHAIRPERSON FROINES: Thanks, Stan.

21 PANEL MEMBER HAMMOND: Bye.

22 CHAIRPERSON FROINES: Paul.

23 PANEL MEMBER BLANC: I'm going to try to build on
24 what Kathi said with perhaps a practical solution that
25 would apply with what she's saying. And, that is, that if

1 the document recommended that the way in which the REL
2 should be interpreted in practice would be that if PM2.5
3 data are available which meet or exceed the REL, then the
4 REL has been met or exceeded; and if PM10 data are
5 available which meet or exceed the REL, then it is
6 incumbent upon the interpreter of the data to then obtain
7 respirable dust-sized collection consistent with the
8 comparable approach. So that you would have an algorithm.
9 Because clearly if you had PM2.5 collections that exceeded
10 the REL, then that's at least -- a particle size that's at
11 least comparable as far as you can tell with --

12 PANEL MEMBER HAMMOND: No, you would -- the PM2.5
13 would underestimate.

14 PANEL MEMBER BLANC: I understand that. I'm
15 saying -- so it's got to be at least -- the PM2.5 would
16 underestimate. It would be too conservative, right,
17 because --

18 PANEL MEMBER HAMMOND: It would be insufficiently
19 conservative.

20 PANEL MEMBER BLANC: It would be
21 insufficiently -- yes, that's what I'm saying. So if you
22 had a PM2.5 results which were higher than the REL, you'd
23 say you've certainly exceeded the REL.

24 PANEL MEMBER HAMMOND: Yes, there's no question.

25 PANEL MEMBER BLANC: If you have PM10, which

1 exceed the REL, then you're obliged to obtain respirable
2 range --

3 PANEL MEMBER HAMMOND: Either control it to bring
4 the PM10 below --

5 PANEL MEMBER BLANC: What's that?

6 PANEL MEMBER HAMMOND: Either control it to bring
7 the PM10 below the REL or measure the respirable.

8 PANEL MEMBER BLANC: Well, we don't suggest the
9 control strategies. The REL is just an action. But it's
10 like an action level. What I'm suggesting is sort of an
11 action level strategy given the realities of what people
12 collect, which is either PM2.5 or PM10.

13 One of the weaknesses of your response was it
14 actually never mentioned PM2.5 in your responses. It was
15 as if that didn't exist. It was as if the choice was PM10
16 or nothing. So people are going to have some PM10 data,
17 they're going to have some -- you know, air districts are
18 going to have PM2.5 data now. And if they wanted to do as
19 a screen, then 2.5. But the 2.5 is under than the PM --
20 it doesn't -- no, that's not true. Take that back.

21 Anyway, you could develop a logical algorithm
22 rather than trying to pretend that PM10 is the same
23 particle distribution and box yourself into that. And I
24 know it would be unusual. It would be the only REL that,
25 you know, talked about things in that way. But it's an

1 unusual circumstance.

2 PANEL MEMBER HAMMOND: But basically what that
3 would come down to is -- if the PM2.5 value were greater
4 than the REL, you know you have a problem.

5 PANEL MEMBER BLANC: Right.

6 PANEL MEMBER HAMMOND: If the PM10 is less than
7 the REL, you know you're okay.

8 PANEL MEMBER BLANC: Yes.

9 PANEL MEMBER HAMMOND: And the problem -- but if
10 it's something other than that, that's where you're going
11 to have to go to get more detailed information.

12 CHAIRPERSON FROINES: But I think it's extremely
13 important to recognize that the PM10 data is not an
14 adequate measure vis-a-vis the REL. And, you know, the
15 South Coast Air Quality Management District and the Bay
16 Area Management District and these people who want bright
17 lines want bright lines. And you cannot use a PM10
18 sampler to measure silica, period.

19 So Paul's -- I agree and disagree with Paul's
20 comments. Paul says if you are at the PM -- if you're at
21 the REL using a PM10 sampler, you may be overestimating
22 it. I think by definition you will overestimate it. And
23 you have no idea how much you're overestimating it by.
24 So, therefore, you can't use it. There's no quantitative
25 validity whatsoever.

1 PANEL MEMBER BLANC: Suppose it was negative?

2 CHAIRPERSON FROINES: If it's negative --

3 PANEL MEMBER HAMMOND: But, no -- if PM10 had a
4 silica under the REL, you're okay.

5 PANEL MEMBER BLANC: You're okay.

6 CHAIRPERSON FROINES: If it's under the -- if the
7 PM10 silica were under the REL, that's okay. But I don't
8 know what it tells you.

9 PANEL MEMBER HAMMOND: That's it. But I think --
10 but I would be -- personally, I'd be afraid that that may
11 not happen because of natural material, but that's larger.
12 But if that happened, it would be great.

13 SUPERVISING TOXICOLOGIST MARTY: Well, maybe I
14 can make this really simple and just say for our -- the
15 purposes of our REL we will set the REL for occupationally
16 respirable -- respirable as defined occupationally. And
17 the rest of the problem really doesn't fall on OEHHA. It
18 falls on ARB and the districts to figure out how they're
19 then going to estimate the emissions from these types of
20 facilities that are in the appropriate size fraction.

21 CHAIRPERSON FROINES: But I think -- Okay, I
22 think that's fine. But I think you have to say, and you'd
23 have to be very clear in your document, and tell people
24 how things change the cube and so on and so forth, so that
25 everybody's clear on -- you get people who are engineers,

1 are not necessarily aerosol scientists, who need to
2 understand it at a very relatively, you know, primary
3 level.

4 PANEL MEMBER BLANC: Couldn't you do that as an
5 appendix that's part of the document, you know --

6 CHAIRPERSON FROINES: Sure.

7 PANEL MEMBER BLANC: -- an example of how you
8 might use this practically or something?

9 SUPERVISING TOXICOLOGIST MARTY: Well, we
10 could -- yeah, what we can do is discuss the issues with
11 using PM10 or using PM2.5. And in fact --

12 PANEL MEMBER HAMMOND: And why they're limited.

13 SUPERVISING TOXICOLOGIST MARTY: -- the comments
14 that we got did a pretty good job of discussing what the
15 problem with PM10 is.

16 PANEL MEMBER BYUS: But you do say up here it
17 will not result in a serious overestimation. And that's
18 not correct. I mean you say it in your document, you say
19 it up here. The tone is completely incorrect, and you
20 really have to fix that.

21 SUPERVISING TOXICOLOGIST MARTY: Yeah. Okay.

22 So we'll take that back. Well, in the final
23 draft of the response to comments, the response to that
24 comment will now be very different --

25 PANEL MEMBER BYUS: Okay.

1 CHAIRPERSON FROINES: And Paul's suggestion is a
2 good one. It does clearly have a limitation at the PM10
3 level. And I can tell you -- I think we all can tell you
4 that there's no quick fix, and that's the problem. And so
5 I think -- I personally think that the -- you know, that
6 your studies that range from 3, 4, 6 -- I don't know how
7 much a 2.5 measure sampler is going to underestimate, but
8 I think the 2.5 sampler is the best solution to the
9 problem that we have at a practical level, understanding
10 that it's an underestimate.

11 PANEL MEMBER HAMMOND: Yes, it's this much. That
12 is the area between those two curves.

13 CHAIRPERSON FROINES: No, I understand. I
14 mean --

15 PANEL MEMBER HAMMOND: And it depends on what the
16 actual size distribution is.

17 CHAIRPERSON FROINES: Absolutely.

18 SUPERVISING TOXICOLOGIST MARTY: I have to say,
19 the more we thought about it, the more we disliked our own
20 response to the comment.

21 PANEL MEMBER BLANC: Now, does this finish up
22 your part of the things you wanted to respond to here? Is
23 this the end of your slides?

24 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
25 SALMON: Yes.

1 PANEL MEMBER BLANC: Because I think that there
2 are a few other things that should -- need to be cleaned
3 up.

4 CHAIRPERSON FROINES: So now we should -- we've
5 actually finished the formal presentation. So we'll go to
6 the leads, who have been silent so far, namely Blanc and
7 Hammond.

8 Paul, go ahead.

9 PANEL MEMBER BLANC: Well, one thing -- one
10 comment that was made is that it's a problem really to use
11 a study from coal miners in this document. And I would
12 agree with that. I think you have enough data without the
13 data from those Chinese coal mine --

14 STAFF TOXICOLOGIST COLLINS: Tin miners?

15 PANEL MEMBER BLANC: I'm sorry. There was a coal
16 mine study, too. I forgot where that was from. I'll come
17 back to the tin mines in a second.

18 They have both exposures, so I don't know how you
19 could interpret a coal mine study. So I just would take
20 it out.

21 The second comment is on the tin miners. Since
22 tin miners get a radiographic -- get radiographic changes
23 related to tin as well as radiographic changes related to
24 silica that's called stenosis, it doesn't have physiologic
25 implications. But it seems that it would add a margin of

1 error into the -- an element of error into interpreting
2 those results. I haven't read the paper that you used. I
3 don't know how they discussed that in there.

4 STAFF TOXICOLOGIST COLLINS: I don't think they
5 did.

6 PANEL MEMBER BLANC: And I was surprised that the
7 consultants who had gone through this with a fine-tooth
8 comb didn't raise that as an issue.

9 And then in terms of other cohort studies, was
10 there -- the slate studies from England -- slate worker
11 studies, did those not have the data in a format that
12 were --

13 STAFF TOXICOLOGIST COLLINS: I'm not sure. Who
14 did those? I'm not familiar with those.

15 PANEL MEMBER BLANC: There were classic studies
16 on silicosis in slate miners in Wales.

17 PANEL MEMBER HAMMOND: I think they didn't have
18 much exposure --

19 PANEL MEMBER BLANC: Well, maybe that's why. But
20 I didn't see it -- I didn't see it dismissed as saying,
21 "Well, you know, we looked at that study and I wasn't
22 as" --

23 STAFF TOXICOLOGIST COLLINS: I don't think we
24 did.

25 PANEL MEMBER BLANC: So could you -- you should

1 pull -- I'm sorry I don't have a citation to give you.

2 SUPERVISING TOXICOLOGIST MARTY: We'll find it.

3 PANEL MEMBER BLANC: The second major thing that
4 I think needs to be brought up to speed in a document,
5 even though you have a section where you say why is it
6 that you're not going to look at lung function, you're
7 only looking at radiographic changes. I think that you
8 should cite the recent American Thoracic Society statement
9 on burden of airway disease related to occupational
10 exposures, in which an analysis of COPD in relationship to
11 dusty trades, which would include silica exposure jobs,
12 is -- should be alluded to in passing. I don't think you
13 need to have a whole section on --

14 STAFF TOXICOLOGIST COLLINS: Something more
15 recent than 1997?

16 PANEL MEMBER BLANC: It's 2004 or 2003.

17 So that needs to be cited. And if you look at
18 the references there, those will probably include some
19 other references that are relevant. There's actually a
20 pretty detailed reference from somebody named Oxman, I
21 think, on dust years of exposure and obstructive lung
22 disease, which includes a lot of silica exposure. And I
23 think you need to allude to that literature even as you're
24 saying we're not going to deal with this.

25 I think another issue that needs to be raised is

1 that you're inherently conservative in the other direction
2 by relying on ILO-graded x-rays that are one over one,
3 because an ILO-graded chest radiograph that's one over
4 zero is, more probable than not, disease.

5 An the ILO system was not invented as a clinical
6 diagnostic tool and it's not to be used clinically
7 diagnostically. It's to be used in epidemiologic studies.
8 And, therefore, it is quite controversial. Although there
9 have been statements saying that one over one is disease
10 and one over zero is not disease, from a public health
11 protective epidemiologic analysis point of view, one over
12 zero is abnormal, and you're using one over one. Now, I'm
13 not telling you to go back and redo everything. But it is
14 a point towards saying, "What we've done, if anything, is
15 not overly conservative." And I think you need to make
16 that point.

17 Another thing that you need to say at some point
18 in a general sense -- or at the same point where I think
19 you need to say that the ILO is not a clinical tool is
20 that, in fact, in this day and age silicosis is typically
21 diagnosed by high resolution CT scanning, which is far
22 more sensitive than plain chest x-rays.

23 And one of the reasons why in these studies when
24 they do autopsies on people who had, quote-unquote,
25 "negative" chest x-rays or chest x-rays that were less

1 than one over one is because it's acknowledged that chest
2 x-rays are not sensitive to detecting disease, and that by
3 CT scanning a lot of those people would have disease.

4 And all the argument about, you know, just
5 because somebody has silicosis at autopsy, is that really
6 a disease? I mean that was a sort of fallacious argument.
7 Now, you don't have to get into that. You did that in the
8 responses. But I think from the other point of view, you
9 need to -- there needs to be some few sentences at least
10 about that.

11 Another point that I think is important, and it
12 relates to your very brief discussion about children or
13 at-risk groups, but this also is relevant to the use of a
14 threefold safety figure rather than one to one, you never
15 discuss anywhere in this document the effect of silica on
16 macrophage function and the risk of tuberculosis related
17 to silica inhalation.

18 It's been very well shown after the South African
19 mines that people without evidence of silicosis by chest
20 x-ray but who have heavy burdens of silica by inhalation
21 are at increased risk of TB and their increased risk of TB
22 and atypical TB multiplied with their HIV status.

23 So if you want to make an argument that there are
24 high risk groups for ambient silica exposure or at least
25 in biological plausibility, I think that the issue of the

1 impact of silica on macrophage function and immune defense
2 systems has to be included.

3 In fact, if you have heavy silica exposure and
4 are PPD positive, you know, that was a reason to prophylax
5 with INH. You didn't have to have silicosis by your chest
6 x-ray, you just had to have a history of silica exposure.
7 So unless I've gotten the criteria wrong, those criteria
8 have been evolving over time. So I think that's
9 important.

10 Then, finally, the -- because this could come
11 back to haunt you in other areas, I think the discussion
12 on the background incidence of chest x-ray abnormalities
13 graded by high or low criteria, which you get into, and
14 you didn't put a slide up, but the critique that the
15 no-effect-level dose in the diatomaceous earth workers was
16 in effect -- was a low effect level because they treated
17 it as the value.

18 But in fact, you know, a 2-over-20 chest x-ray
19 shouldn't be abnormal. And then you sort of say, "Well,
20 we realize that smoking and age are related to ILO
21 criteria." Then you say that the incidence based on, you
22 know, the chest -- the general chest analysis is two
23 percent in North America. There are real problems with
24 that paper and that analysis.

25 And this is going to come back and bother you in

1 other situations. You have accepted on face value an
2 analysis which was extremely flawed. And, in fact, the
3 Castellan study, which you cite, is the only study that's
4 ever been done intentionally to test the hypothesis, you
5 know, "What is the incidence of ILO-read abnormalities in
6 non-exposed people?" And his value was .2 percent or some
7 number like that.

8 You need either to go -- you need to go back and
9 read the original articles, including Castellan. And
10 don't just cite that supposed meta-analysis on face value.
11 I'm going to give you a couple of articles that are
12 relevant.

13 STAFF TOXICOLOGIST COLLINS: Is that Blanc and
14 Gamsu?

15 PANEL MEMBER BLANC: Yeah. And a second one.

16 This is going to be extra work for you guys.
17 But, in fact, it's going to be useful for you I think in
18 other situations. And I think it's just worth it for the
19 Agency to come up with a -- now, you may come to a
20 different conclusion than I have in reviewing that
21 literature. But at least you've got to invest the time to
22 do it because it's quite an important issue.

23 And I don't agree with your conclusions. I
24 don't -- a) I don't -- except for asbestos exposure where
25 clearly smoking was related to ILO-graded opacities in a

1 multiplicative way with asbestos. There's no other
2 occupational data that suggests that when it's been
3 analyzed correctly.

4 So that's the bulk of my comments.

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

6 SALMON: Thank you.

7 One very small point. I think we recognize what
8 you're pointing out, that the ILO grading that we were
9 using as a trigger point is a relatively severe effect.
10 And that is certainly factored into our decision to use a
11 BMD01, recognizing that the effects that we were using as
12 a benchmark is by any reasonable standards a fairly severe
13 effect, as opposed to a BMD05, which is, you know,
14 defaults for -- or standard for mild effects, which is of
15 some significance.

16 PANEL MEMBER BLANC: Okay. You actually didn't
17 say that as clearly in the document, because basically
18 what you say is "We know that silicosis is an effect."
19 But you didn't say, in fact, "This is not just silicosis.
20 This is hit-you-over-the-head silicosis."

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: That's something we ought to clarify.

23 PANEL MEMBER BLANC: Right, because were we to
24 use silicosis defined by one over zero or silicosis
25 defined by CT scanning, which in clinical practice is what

1 people would use, we would -- you know, that would be a --
2 probably a milder disease. And by the time it's one over
3 one, you know --

4 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

5 SALMON: It's incontrovertible.

6 PANEL MEMBER BLANC: Right. Now, that is one
7 reason why the silicosis -- you know, you say there is one
8 study where you're using silicosis where the majority of
9 the silicosis is from death certificates. But I would
10 make the argument that silicosis by death certificate is
11 even worse than one over one, because for somebody to get
12 silicosis on their death certificate -- I thought the
13 argument was completely not convincing from the outside
14 critique that -- you know, who cares if there's silicosis
15 on the death certificate. You know, that's over-reported,
16 because they lived in mining districts. I mean every
17 study that's ever been done shows that death certificates
18 underestimate occupational disease.

19 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

20 SALMON: We hope that the REL would be protective before
21 things got to that point.

22 CHAIRPERSON FROINES: Kathi.

23 PANEL MEMBER HAMMOND: I agree with several of
24 Paul's points, I mean particularly -- the way I was going
25 to say it is simply that I think that by using the

1 criteria that you used, you are underestimating the true
2 effect. And I think that that needs to be said clearly.
3 It is in the document, but I think it -- I think it needs
4 to be very clear that there's -- that there is kind of an
5 underestimate, but this is -- if you feel it's true, and I
6 would defer to what Paul says and what, you know -- that
7 if that's the best that we can do now, that's the best we
8 can do. But I think we should be clear that we understand
9 that the effects can be greater.

10 The other thing that I found confusing going
11 through the document is whether or not you were doing just
12 silicosis or other lung disease. And I think it's just
13 silicosis. It's all being done that way. But you have a
14 sentence, for instance, on page 6 which says, "At one
15 microgram per cubic meter silica the excess lifetime risk
16 was estimated to be 1.6 cases of lung disease other than
17 cancer for a thousand workers." And then you go to a
18 table that is silicosis.

19 And, you know, I think if it's just -- maybe
20 again you might want to say there are these other diseases
21 you think are associated. And you may not be being
22 protective. That may be something -- there may just be
23 insufficient data to protect from COPD. But I think that
24 at some point you may want to just -- and, again, Paul may
25 know now to do that better than I. But somehow

1 specifically address there are these other diseases and
2 the reasons you've not addressed them, which may be the
3 lack of data.

4 But then through the rest, as I say, we're doing
5 just silicosis. And we're kind of doing just silicosis as
6 it's pretty far along the way, and so we're
7 underestimating the true number of cases.

8 And that's how I would see it.

9 PANEL MEMBER BLANC: I have an algebraic question
10 for you, too.

11 When you go from a work exposure to environmental
12 exposure, you have a mathematical adjustment that you do
13 for the hours of exposure being 40 hours a week to being 7
14 days a week; isn't that correct?

15 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
16 SALMON: The way it works, we actually weight the hours
17 during the day more strongly. Because what we do is we
18 actually assume that during your work time you inhale 10
19 of your allotted 20 cubic meters, rather than saying it's
20 8 hours out of the 24.

21 PANEL MEMBER BLANC: Right. So here's my point
22 about Sluis-Cremer and Hnizdo. And maybe Dr. Hnizdo can
23 clarify this for you. I do not believe that the
24 underground miners in South Africa worked from 9 to 5, 5
25 days a week. I really don't think that's true. I think

1 at a minimum there was a 6-day work week. Now, whether it
2 was a 12-hour shift or a 10-hour shift, she could clarify
3 for you. But I do think it's going to impact a little bit
4 your number.

5 STAFF TOXICOLOGIST COLLINS: We have a
6 clarification from her. And I think she made everything
7 equivalent to an 8-hour work shift. And I'd have to dig
8 that up for you. But I'll -- if I find that, I'll send it
9 to you.

10 PANEL MEMBER BLANC: You mean in her years of
11 exposure, in her dust years of exposure? I mean what do
12 you mean she did it?

13 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

14 SALMON: Her calculation is a cumulative dust exposure.

15 PANEL MEMBER BLANC: So that if you worked a year
16 in the mines, that was like one and a quarter years of a
17 normal person?

18 PANEL MEMBER HAMMOND: An American.

19 PANEL MEMBER BLANC: Of an American person? I'm
20 sorry.

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: I think, in essence, what we're -- the impression
23 we have from Dr. Hnizdo is that they, so to speak,
24 normalized the actual hours of exposure that were thought
25 to have occurred, as if a standard shift would have been

1 in operation.

2 PANEL MEMBER BLANC: I think you need to clarify
3 it, because -- I mean the fact that I've changed --

4 STAFF TOXICOLOGIST COLLINS: It's in the text.
5 But, okay.

6 PANEL MEMBER BLANC: -- it's not going to change
7 your calculation. I mean if she -- depending on how she
8 did that, it changed your calculation. Now, it's not
9 going to change it by 50 percent. But, you know, it could
10 change it by 10 percent or something, I mean --

11 SUPERVISING TOXICOLOGIST MARTY: Yeah, she went
12 through the job classification and had average hours in
13 the dust by job classification. But the biggest number on
14 the table is eight. So if in fact it was ten six, days a
15 week, I'm not sure that she adjusted for that.

16 PANEL MEMBER BLANC: You may want to -- I mean
17 one way or the other I think you should have a footnote
18 that says, "We took this into account" or, you know, "We
19 didn't take this into account" or, you know --

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
21 SALMON: It sounds like we need to have another phone call
22 to Dr. Hnizdo.

23 PANEL MEMBER BLANC: I'm going to see her next
24 week. So I could --

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: Warn her we're coming.

2 CHAIRPERSON FROINES: Can we move along?

3 Kathi, are you finished?

4 PANEL MEMBER HAMMOND: (Dr. Hammond nods head.)

5 CHAIRPERSON FROINES: Are there comments from
6 Craig and Joe?

7 Now, the question I would have is -- I have no
8 more -- I don't think we need more comments.

9 The question is -- there have been a lot of
10 suggestions made. And we have two choices. One, we can
11 vote on accepting the document, the REL, as proposed
12 pending changes. Or we can say that we'll postpone the
13 approval pending the changes and take a look at the
14 document again.

15 PANEL MEMBER HAMMOND: I don't -- first of all,
16 what size fraction are we talking about for the REL? What
17 particle size fraction is the REL applicable to? Is it
18 PM10, PM2.5, respirable occupational defined?

19 CHAIRPERSON FROINES: Well, the REL has nothing
20 to do with that.

21 SUPERVISING TOXICOLOGIST MARTY: We would make
22 the change of respirable per -- NIOSH respirable.

23 PANEL MEMBER HAMMOND: Okay. Because I think
24 that would be -- that's like the --

25 CHAIRPERSON FROINES: The issue on the

1 respirability and the PM10 is an issue for -- actually for
2 ARB once they've cleaned up their language that I think
3 Craig or Joe mentioned. But basically I think the
4 REL will -- I don't think there's anything that's been
5 said that would change the REL as proposed.

6 PANEL MEMBER BLANC: I think that there's enough
7 substantive issues here that we need to see another
8 version. I think this is across the threshold to a
9 follow-up version. And I think you feel the same way
10 probably.

11 SUPERVISING TOXICOLOGIST MARTY: Yeah, and
12 particularly since we're going to try to do a better job
13 on the exposure issue. That could change the number. I
14 don't know if it would change substantially, but it will
15 definitely change.

16 CHAIRPERSON FROINES: So let's then -- we won't
17 take a vote. We will take it up as an agenda item at the
18 next meeting in July? Jim --

19 MR. BEHRMANN: We have --

20 CHAIRPERSON FROINES: -- what are we thinking
21 right now in terms of the next meeting date?

22 MR. BEHRMANN: Jim Behrmann, panel liaison.

23 The two days that we've identified were July 21st
24 and 23rd. But I think that may be somewhat dated and the
25 panel needs to check their calendars again.

1 CHAIRPERSON FROINES: Okay. But we're planning
2 to have a summer meeting at some point.

3 And so would you think you would be ready for
4 them, so we assume that it would come back in July?

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
6 SALMON: Yeah, we'll try and do that. I think we can do
7 that.

8 CHAIRPERSON FROINES: Okay. Thanks, folks.

9 So we will hold on that. Is that acceptable to
10 you guys?

11 Okay. The next item on the agenda is Department
12 of Pesticide Regulation. And I want to limit the
13 discussion today on this issue.

14 And, Tobi, you want to sit -- in case there are
15 some questions, do you want to sit here.

16 Basically everybody on the panel has received the
17 little document that Jim and I prepared that sort of lists
18 the history of the relationship with DPR. I suspect Kathi
19 hasn't seen it yet because she's been traveling. Joe's
20 seen it. Craig has seen it. We have three panel members
21 not here. And I don't know about Paul.

22 So if -- I'm here.

23 Have you seen the document I'm talking about?

24 PANEL MEMBER BLANC: Yes.

25 CHAIRPERSON FROINES: Thank you.

1 And so this is background. And I'm not going to
2 say anything more about it at this point.

3 There are clearly unresolved issues that exist
4 between the panel and DPR. And I would propose to the
5 panel that I or a small group of panel members meet with
6 Secretary Tamminen and Director Helliker and talk about
7 some of those issues. And that would be my proposal for
8 what we in part take up -- talk about today.

9 The second issue is -- Tobi's going to mention,
10 is she's looking for some leads for sulfur luoride. And
11 perhaps she could give us an update on the timing of when
12 that's coming forward.

13 The third issue that we've received is the
14 request for a discussion on the prioritization process,
15 which I'm going to take the -- what of the Chair? What do
16 you call it -- the prerogative of the Chair and postpone
17 that till July, because we have -- as I say, we have three
18 people missing. And I think we should take that up when
19 we have a little larger number of people.

20 So at this point I'm really only asking for two
21 things. Can I get agreement on a meeting with the
22 Secretary and the Director to talk about the issues that
23 you would feel comfortable with that happening? Paul at
24 one point had said he thought that it wasn't useful to
25 write more letters. And so I'm suggesting that a meeting

1 between principals that could discuss some of the issues
2 that exist between the parties.

3 PANEL MEMBER BLANC: Sure.

4 CHAIRPERSON FROINES: Everybody talks a lot, and
5 then all of a sudden you get nothing back.

6 PANEL MEMBER HAMMOND: Do you want acclamation?

7 PANEL MEMBER BLANC: Who are you thinking would
8 come from Cal EPA for that?

9 CHAIRPERSON FROINES: The Secretary.

10 PANEL MEMBER BLANC: And would there be someone
11 from OEHHA?

12 CHAIRPERSON FROINES: Yes.

13 PANEL MEMBER BLANC: And who would that be?

14 CHAIRPERSON FROINES: I don't know.

15 PANEL MEMBER BLANC: What level would you like?

16 CHAIRPERSON FROINES: I don't know. I think what
17 I need is flexibility from -- I think that the issue of
18 whether OEHHA attends or not is something that this panel
19 should suggest their views.

20 PANEL MEMBER BLANC: I think it would be very
21 helpful to have somebody from OEHHA there because it might
22 facilitate communications and workload, avoid duplication,
23 and provide encouragement.

24 CHAIRPERSON FROINES: I don't want to exclude the
25 ARB. But I think OEHHA and DPR would be the -- because I

1 think that there is specific interaction that occurs
2 between those two agencies. And my sense is we don't want
3 to make it larger than it really needs to be for this
4 discussion.

5 PANEL MEMBER BLANC: Although, you know, one
6 thing about the ARB and one of the things that has been a
7 theme that's come up repeatedly has been the time line of
8 data monitoring and the integration of data monitoring
9 with proposed toxicity evaluations, where one thing -- you
10 know, one substance is being sampled and another substance
11 is being discussed in terms of a toxic air contaminant.

12 And so however it is -- I mean there definitely
13 should be something on your agenda. And it would be I
14 think important to have -- if the person isn't at the
15 table who ultimately, you know, is in charge of the actual
16 field sampling, there should be some form of communication
17 for that --

18 CHAIRPERSON FROINES: No, I think that should be
19 a subsequent meeting where we talk -- at the meeting that
20 I'm talking about we talk about the larger issues and then
21 have more detail on some of the issues that are very
22 important but not necessarily --

23 PANEL MEMBER BLANC: You're saying some of this
24 other stuff is the sine qua non; and then if you don't
25 have that, then none of the rest of it really matters.

1 CHAIRPERSON FROINES: Well, I think that since
2 the discussion is about the relationship between the panel
3 and DPR, what we don't want is other departments or other
4 agencies to kind of be there and, therefore, in a sense
5 inhibit what should be a smaller discussion, I think.

6 PANEL MEMBER BLANC: A free and frank exchange
7 of --

8 CHAIRPERSON FROINES: -- ideas.

9 PANEL MEMBER BLANC: -- ideas?

10 CHAIRPERSON FROINES: And we'll take up the risk
11 prioritization process.

12 So hearing no objections, I'm going to go ahead
13 with that.

14 Tobi, bring us up to date on the sulfurofluoride
15 issue.

16 DPR ASSISTANT DIRECTOR JONES: We have a draft
17 risk assessment that has gone through external peer review
18 by OEHHA and ARB, currently considering those comments.

19 I had originally laid a tentative schedule in
20 communications with ARB and OEHHA back in December of
21 looking at possibly fall for presenting to the SRP. So we
22 have some -- we have some steps before that in terms of
23 public comment, a public meeting, and that sort of thing.

24 CHAIRPERSON FROINES: There's one thing that --
25 as most -- as everybody on the panel knows, and probably

1 most in the audience don't know, is there was a question
2 raised about the fact -- there was some question raised
3 about my participation in the development of the
4 naphthalene document, and whether a person on this panel
5 should be engaged in the development of a document prior
6 to pursuing it from a peer-review standpoint.

7 In other words, if I'm too deeply involved in,
8 say, naphthalene, does that mean that my ability to serve
9 as a peer reviewer on the SRP is compromised? And so that
10 issue's been raised.

11 That would -- if that issue were to be an
12 important question, it would raise serious doubts about
13 the ability of the panel to have leads working with the
14 agencies.

15 And so, Jim, is it -- my impression from the
16 Secretary's office is they do not consider that an issue
17 because we are a standing committee as opposed to a UC
18 Office of the President peer review person. In other
19 words, if OEHHA or DPR goes to the UC to identify two or
20 three peer reviewers, then that would be relevant to that
21 regulation. But for a standing committee it's not
22 relevant. So my impression is that we should go ahead on
23 the assumption that we can still appoint leads.

24 Is that fair?

25 MR. BEHRMANN: Yes, you can still appoint leads,

1 especially in the case of pesticides, I believe.

2 What you were referring to are the CalEPA
3 guidelines for peer review, which provide that in the case
4 of where an author has been involved in actually drafting
5 a document, that person obviously could not be appointed
6 as an outside peer reviewer for it.

7 But I think that's a separate issue from how this
8 committee as a standing committee uses the idea of leads.

9 CHAIRPERSON FROINES: Okay. So we'll proceed,
10 Tobi, on the assumption that we're free and clear to keep
11 doing things the way we've been doing. Because we have
12 been doing them for -- since 1983, and so -- but obviously
13 the kind of litigated world has changed since 1983, and so
14 you never know where you're going to be.

15 So we need to appoint two people, one of whom
16 would be interested in the exposure issues and the other
17 would be a person who would have the health effects side.

18 Now, in terms of the health effects side, what's
19 driving the risk assessment? Is it epidemiologic data or
20 toxicologic information?

21 DPR ASSISTANT DIRECTOR JONES: Toxicological
22 data.

23 CHAIRPERSON FROINES: Tox data.

24 So do we have any volunteers, assuming this is --

25 PANEL MEMBER BYUS: I have a question.

1 CHAIRPERSON FROINES: Paul and Kathi just
2 finished being leads. So they theoretically have
3 get-out-of-jail-free cards.

4 PANEL MEMBER BYUS: Relative to that question,
5 whatever happened to the cholesterase inhibition
6 document -- that inhibitor document that you were all
7 preparing, of which I was a lead on for some year and a
8 half ago or two years ago -- year and a half ago?

9 CHAIRPERSON FROINES: This is going to guarantee
10 that you're the assigned person, you know.

11 (Laughter.)

12 PANEL MEMBER BYUS: No, no, no. I'm sorry. I
13 was the lead on that document. But I wanted to know where
14 that document is.

15 CHAIRPERSON FROINES: That's my point.

16 PANEL MEMBER BYUS: Okay.

17 DPR ASSISTANT DIRECTOR JONES: The project has
18 not died. But as far as the document relative to this
19 committee, I will refer back to the Chair and
20 communications that my Director has had with the Chair and
21 correspondence.

22 PANEL MEMBER BYUS: I didn't know that --

23 CHAIRPERSON FROINES: As far as -- the
24 correspondence from Director Helliker basically said that
25 that was one of the areas that they would no longer

1 interact with the panel on. And so that's where that is.
2 That's clearly one of the issues that we would still like
3 to be involved in and so would like to talk about that
4 further.

5 So does that mean that you'd be willing to serve
6 as the sulfurofluoride lead?

7 PANEL MEMBER BYUS: Sure, I suppose.

8 CHAIRPERSON FROINES: Well, Joe's just done
9 formaldehyde. And so by process of elimination --

10 PANEL MEMBER BYUS: If you think.

11 CHAIRPERSON FROINES: And then I would -- since
12 Roger's not here, let's appoint Roger to be the exposure
13 person.

14 PANEL MEMBER BLANC: Good.

15 CHAIRPERSON FROINES: There's very little
16 democracy in this. But I did ask for volunteers first.

17 PANEL MEMBER BYUS: Sure.

18 CHAIRPERSON FROINES: So Tobi, Craig, and Roger.

19 DPR ASSISTANT DIRECTOR JONES: Okay. All right.
20 Thank you.

21 CHAIRPERSON FROINES: I should say that I talked
22 with Shankar Prasad today. And I don't know whether this
23 is confidential and I'm breaking a confidence, but there
24 is movement on replacing Peter Witschi. And so we may
25 have another panel member in the foreseeable future.

1 So that's good. That will be -- because
2 that's -- that position is the position of a pathologist.
3 So it would add some more toxicology expertise to the
4 panel.

5 Did you have a sense of when -- the other
6 document -- I don't remember. There was a second chemical
7 listed that was going to be later. Was that chlorpiriphos
8 or --

9 DPR ASSISTANT DIRECTOR JONES: No, that was
10 athidithion.

11 CHAIRPERSON FROINES: Do you have any dates?

12 DPR ASSISTANT DIRECTOR JONES: No, I'm sorry, I
13 don't. But it is -- in terms of our processing of the
14 Director's assessment and working with OEHHA and ARB, it's
15 on a similar track. So I would say it would come in
16 behind sulfurofluoride. It would come in behind
17 sulfurofluoride.

18 CHAIRPERSON FROINES: Okay. So I think that's it
19 for now. We'll take up the risk prioritization document
20 in June -- in July. And then we'll try and talk with
21 Helliker and Terry Tamminen, and then we'll go from there.

22 Thanks, Tobi.

23 DPR ASSISTANT DIRECTOR JONES: Thank you.

24 CHAIRPERSON FROINES: Sorry to keep you all day.

25 DPR ASSISTANT DIRECTOR JONES: That's okay.

1 CHAIRPERSON FROINES: Finally, who is the ETS
2 person, who's lucky to have Stan having dropped off --

3 MR. KRIEGER: Good afternoon, Dr. Froines and
4 members of the Panel. My name is Robert Krieger. I am
5 lead staff for the ETS party exposure assessment.

6 Today I'll just be giving you a brief update on
7 the status of where we are in our ETS report.

8 As you know, in December 2003 we released a
9 public version of a report for a 90-day comment period
10 which ended March 29th. We also had a public workshop on
11 the report on March 15th, which some of you were in
12 attendance.

13 To date we have received 25 comment letters, 14
14 of which are health related, 8 are exposure related, and 9
15 comment letters are supportive of our report and our
16 program as well.

17 Currently both ARB and OEHHA staff are in the
18 process of summarizing and responding to these public
19 comments. Our next test will be to prepare a Part C of
20 the report, which addresses the comments, as well as
21 update Parts A and B of the report where appropriate.

22 We plan to take the revised Part A, Part B, and
23 Part C available to the Scientific Review Panel for formal
24 review in time for a meeting in September if one can be
25 arranged at that time.

1 And that's basically our update on ETS.

2 CHAIRPERSON FROINES: So you're planning for the
3 panel to take it up in September?

4 MR. KRIEGER: Yes, the formal review of the whole
5 revised Parts A, B, and C in September.

6 CHAIRPERSON FROINES: And the panel will receive
7 the comments and your response to comments.

8 MR. KRIEGER: Oh, that will be in August. They
9 won't be in September at the meeting. But you'll get
10 plenty of time to review those, report and comments before
11 the meeting.

12 CHAIRPERSON FROINES: This is going to be a lot
13 of material that people are going to be looking at. So
14 the earlier, the better I think for all of us.

15 I think that -- you know, you saw today that we
16 had at least two people who just came back from long
17 trips. We had Roger, who was teaching. And so given the
18 fact that this is a group of people who meet relatively
19 infrequently but have very, very busy schedules, the
20 sooner that everybody gets a complete package I think the
21 better.

22 Paul.

23 PANEL MEMBER BLANC: That's true. We're so
24 important.

25 (Laughter.)

1 PANEL MEMBER BYUS: That's why we get paid so
2 much.

3 (Laughter.)

4 CHAIRPERSON FROINES: I haven't heard the
5 Governor was going to plan a new bond so we can get a
6 higher pay.

7 So it looks like we're about to do it in
8 September.

9 MR. KRIEGER: Yes.

10 CHAIRPERSON FROINES: And you finished your
11 monitoring for -- you finished the exposure piece?

12 MR. KRIEGER: Yes, the monitoring's complete.
13 It's in our current version right now.

14 CHAIRPERSON FROINES: Okay. Thanks.

15 MR. KRIEGER: Thank you.

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

18 CHAIRPERSON FROINES: One other item -- just one
19 other item is that the diesel suit will be heard as far as
20 we know at the end of June.

21 Right, Jim? What's the date?

22 PANEL MEMBER HAMMOND: We need a closed session
23 for this.

24 CHAIRPERSON FROINES: No, this is information.

25 No, we don't need -- why don't we just not take

1 this up.

2 MR. BEHRMANN: Actually if you were just going to
3 speak about dates, that would not necessitate a closed
4 session. There will be a one-day trial toward the end of
5 June. And in that case there are some exchanging briefs
6 at this time.

7 CHAIRPERSON FROINES: That's sufficient.

8 MR. BEHRMANN: I could ask Kirk at the next
9 meeting to give a more detailed update, and that could be
10 done in a closed session then.

11 CHAIRPERSON FROINES: Well, next meeting is --
12 it's theoretically past tense, so that --

13 PANEL MEMBER BLANC: Well, it would be a better
14 update then.

15 (Laughter.)

16 CHAIRPERSON FROINES: Okay, Paul. Make a motion.

17 PANEL MEMBER BLANC: I move that we adjourn.

18 PANEL MEMBER BYUS: Second.

19 CHAIRPERSON FROINES: All in favor?

20 (Ayes.)

21 CHAIRPERSON FROINES: Meeting is officially
22 adjourned.

23 (Thereupon the California Air Resources
24 Board, Scientific Review Panel adjourned
25 at 4:10 p.m.)

1 CERTIFICATE OF REPORTER

2 I, JAMES F. PETERS, a Certified Shorthand
3 Reporter of the State of California, and Registered
4 Professional Reporter, do hereby certify:

5 That I am a disinterested person herein; that the
6 foregoing California Air Resources Board, Scientific
7 Review Panel meeting was reported in shorthand by me,
8 James F. Peters, a Certified Shorthand Reporter of the
9 State of California, and thereafter transcribed into
10 typewriting.

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

14 IN WITNESS WHEREOF, I have hereunto set my hand
15 this 28th day of May, 2004.

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22 JAMES F. PETERS, CSR, RPR

23 Certified Shorthand Reporter

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