

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

SOUTH SAN FRANCISCO CONFERENCE CENTER
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SOUTH SAN FRANCISCO, CALIFORNIA

WEDNESDAY, NOVEMBER 28, 2001

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APPEARANCES

MEMBERS PRESENT

Dr. John Froines, Chairperson

Dr. Roger Atkinson

Dr. Paul D. Blanc

Dr. Craig Byus

Dr. Gary Friedman

Dr. Anthony Fucaloro

Dr. Hanspeter Witschi

Dr. Ellinor Fanning

REPRESENTING THE CALIFORNIA AIR RESOURCES BOARD

Mr. Jim Behrmann

Mr. Peter Mathews

REPRESENTING THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD
ASSESSMENT

Dr. George V. Alexeef, Deputy Director for Scientific
Affairs

Mr. David Lewis, Staff Toxicologist

Mr. David Morry, Staff Toxicologist

Dr. David Rice, Staff Toxicologists

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

REPRESENTING THE DEPARTMENT OF PESTICIDE REGULATION

Dr. Keith Pfeifer, Pharm.D, Ph.D., DABT, Senior
Toxicologist

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1 PROCEEDINGS

2 CHAIRPERSON FROINES: We need to start given the
3 fact that two people have to leave at 2:00 o'clock.

4 PANEL MEMBER FUCALORO: Three.

5 CHAIRPERSON FROINES: Pardon me?

6 PANEL MEMBER FUCALORO: Three people have to
7 leave.

8 CHAIRPERSON FROINES: Who are the three?

9 PANEL MEMBER FUCALORO: Craig, I and Roger have
10 to leave.

11 CHAIRPERSON FROINES: And Peter. So at 2:00
12 o'clock the meeting will end. We don't have really any
13 choice. So I think we should begin. Now, we should have
14 a brief discussion, at some point, about travel issues,
15 but I think that given the fact that Gary and Paul aren't
16 here, we probably shouldn't start with that because that
17 would create a southern California bias.

18 PANEL MEMBER FUCALORO: B-i-a-s as opposed to
19 B-y-u-s.

20 (Laughter.)

21 CHAIRPERSON FROINES: So anyway, we should
22 officially open the meeting on November 28th, 2001 of the
23 scientific review panel. And let's begin following the
24 agenda and discuss at the outset the chronic REL issues
25 that OEHHA is going to be bringing forward.

1 Andy.

2 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

3 SALMON: Thank you. I thought I'd just start because we
4 haven't been talking about the RELs for some little while
5 now. I though I'd just remind you where we've got to with
6 the noncancer chronic RELs.

7 (Thereupon an overhead presentation was
8 presented as follows.)

9 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

10 SALMON: We have been working on the review of the
11 compound specific summaries and the proposed RELs. The
12 methodology guidelines were reviewed by the panel and
13 adopted in February of 2000.

14 We have had a first batch of RELs, which was
15 included with the guidelines. Then two further addenda,
16 which included additional RELs. And we're now in the
17 process of dealing with an additional batch, which we're
18 calling batch 2B.

19 --o0o--

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

21 SALMON: You saw this initially on March the 5th and we
22 haven't had any opportunity to do anything with it until
23 now. But basically what we're doing is we received some
24 public comments which we have responded to and
25 incorporated any additional information which came up

1 But anyway, so this is a particularly new item in this
2 series.

3 --o0o--

4 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

5 SALMON: So these are the ones that we're actually going
6 to be presenting today, and there are some which we have
7 decided we can't deal with today because we were unable to
8 complete the update and review to our satisfaction and --
9 mainly due to our -- well, when we went back and looked at
10 the requirements of the panel and the requirements of the
11 SB 25, we identified the fact that we did not have
12 sufficient data available or methodology available to
13 resolve the issue.

14 So in the case of ethylene glycol butyl ether or
15 butoxy ethanol, one of the questions which the panel
16 identified was that we should look at the dose response
17 for irritancy. And this has clearly important for the
18 suitability of the REL for protecting adult health, but
19 it's particularly important for considerations of
20 children's health as well.

21 And, at this point, we've not been able to
22 identify satisfactory data or methodology for dealing with
23 this, so we're going to have to work on this some more.

24 We've also not brought forward a revision of the
25 fluoride REL, at this point, because we need to work out

1 with the Air Board, the exposure assessment people,
2 whether this needs to be treated as a multi-media
3 chemical. And if it does need to be, then as fluoride
4 salts at least, may need to be -- then we need an oral REL
5 as well as the inhalation REL.

6 Nitric acid --

7 CHAIRPERSON FROINES: Andy, would you say that
8 again, about the fluoride issue?

9 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

10 SALMON: The fluoride issue is the REL which we have
11 proposed is basically a straightforward inhalation REL
12 which has applicable vapor phase chemicals. But fluoride
13 salts, in particular, of course, you know, it may
14 initially be emitted as a particulate material or else
15 become a particulate material in the course of atmospheric
16 reactions.

17 And if it then is in particulate form, it may
18 sediment out of the atmosphere, deposit on crops, deposit
19 on soil and things like that. And for materials which
20 behave like that, we need to provide an oral REL, which is
21 used in the multi-media analysis defined by the hot spots
22 exposure assessment guidelines, and there are certain
23 chemicals which are identified as potentially needing a
24 multi-media analysis.

25 And so if it is concluded that emissions of

1 actually or potentially particulate fluoride is an issue
2 in California, it certainly is some in other areas, things
3 like brick works for instance are notorious for emitting
4 particulate fluoride salts in some areas.

5 PANEL MEMBER FUCALORO: And this is way above
6 what one would normally get in fluoridated water or
7 toothpaste.

8 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

9 SALMON: Depending on circumstances. There are examples
10 in the world where there is at least locally a problem. I
11 think the issue is whether that's important in California.

12 PANEL MEMBER ATKINSON: So how would you relate
13 the, let's say, the atmospheric particle concentration of
14 fluorides to what would be on soil or plants? I mean,
15 there may be no relation whatsoever.

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

17 SALMON: There's only an indirect relationship. There's a
18 methodology for dealing -- which is a sort of default
19 approach, for dealing with multi-media chemicals, which is
20 in the Part 4 hot spots guidelines which you reviewed
21 fairly recently.

22 It uses various sorts of atmospheric modeling to
23 handle the way the emissions are distributed and
24 potentially deposited. So I'm not saying that it answers
25 all the questions that might be asked, but it's an

1 approach which is used to determine whether or not there
2 might be a problem there at least.

3 Clearly, this can be a very complex issue, but
4 the question we have, at this point, is whether we need to
5 include fluorides in that approach. And if so, then we
6 need to develop an oral, as well as, an inhalation REL.

7 CHAIRPERSON FROINES: Do you have a sense --

8 PANEL MEMBER ATKINSON: We do have almost done a
9 couple of almost, a couple of inhalation from the oral.
10 It's the oral where you depend upon the concentration of
11 the fluoride and whatever you're getting it from.

12 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
13 SALMON: It might be we should develop separate RELs for
14 hydrogen fluoride and other fluorides versus fluoride
15 salts which would be particulates. Certainly, I mean we
16 will look into that.

17 CHAIRPERSON FROINES: Do you have a sense that
18 there is still a continuing use of hydrogen fluoride in
19 the petroleum refinery?

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
21 SALMON: It's my understanding that there is some
22 continuing use. I don't know that -- it's my
23 understanding that some refineries are moving away from
24 that, but the last time we checked the emissions data
25 there was, you know, there were real numbers there. May

1 be if we come out with this REL, it might accelerate that
2 transition who knows.

3 CHAIRPERSON FROINES: Has ARB or the local air
4 districts done monitoring so that there is a database?

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
6 SALMON: There are data on fluoride emissions in the hot
7 spots database, yes.

8 The next one that we are not presenting today,
9 which you have actually seen previously, it was nitric
10 acid. And what we did here was we did a fairly standard
11 analysis using, unfortunately, some rather old animal
12 studies on nitric acid effects, and came up with a
13 proposed REL which, you know, looks reasonable from the
14 methodological point of view.

15 But when we examined this from the point of view
16 of our SB 25 evaluation, we realized that there is a very
17 significant problem with acid aerosols and the
18 exacerbation of asthma, which is a big problem for
19 children. I'm going to be discussing this a little bit
20 more when I come to present sulfuric acid REL.

21 But the situation of the nitric acid was that it
22 was fairly clear that the REL which we had using data
23 available for nitric acid would not be protective of the
24 children's health in relation to exacerbation of asthma by
25 acid aerosols, if that is a problem with nitric acid, and

1 it seemed reasonable to us to suppose that it might be.
2 So we're going to have to go back and do some more work on
3 this one and figure out how to include that consideration.

4 The phosphine REL, there is a question of how we
5 defined the NOAEL and which endpoint we're using. And we
6 have to review those questions, again, in light of the
7 fact that there are several potential endpoints with
8 slightly different NOAELs, different quality of data in
9 the experimental record and some implications for some of
10 those endpoints needing to be further considered under SB
11 25 guidance. So we're, again, holding that one back so we
12 can do more work on it.

13 And the final one, triethylamine, again, the end
14 point is basically irritancy. And this will be apparent,
15 I think, with the next group of chemicals. And when I do
16 present the RELs, that irritancy appears to be quite an
17 important and a fairly common endpoint. And there are
18 implications which we need to consider in terms of the
19 impact on children's health.

20 And in the particular case of triethylamine,
21 there appears to be an inconsistency between animal and
22 human data, which we're still trying to resolve. So this
23 one we've proposed to defer.

24 I'll now start on the ones that we actually are
25 going to present. And the first one of these is -- it's

1 been pointed out to me that the lead on this chemical was
2 Dr. Blanc. And given that he is not here at the moment --
3 but I assume maybe later -- the suggestion was, Mr.
4 Chairman, whether you would want us to defer consideration
5 of this particular one until he's here?

6 CHAIRPERSON FROINES: No, go ahead. I think that
7 it will be fine.

8 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
9 SALMON: Okay. This is the basis of the REL which you
10 have seen fairly similarly presented before. We haven't
11 changed the key study, but what we have done is that we
12 have actually gone back to the original data from that
13 study which we obtained after a rather torturous process
14 of inquiry through the federal agencies.

15 And we've actually now calculated a benchmark
16 concentration, BMC05, which is the benchmark which we are
17 proposing to use regularly for this sort of analysis. So
18 the modification here, firstly, is the calculation of the
19 new benchmark from the raw data in the study.

20 We also looked at some other information. There
21 was another study in the literature that looked as if it
22 might be informative, but we were not able to actually get
23 the original raw data, so we couldn't do the calculation,
24 but that's available as a comparison.

25 And additionally, we have considered the

1 implications of carbon disulfide toxicity for children's
2 health. And obviously this was reviewed in the SB 25
3 document, which you've just finished working through.

4 --o0o--

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
6 SALMON: The situation that we identified there was that
7 there was some specific concerns about carbon disulfide,
8 but it didn't quite reach the level of concern where we
9 could actually identify a differential impact. So we
10 haven't proposed changing the REL to reflect any such
11 differential impact on infants and children, but we do
12 review some of our remaining concerns.

13 We've also incorporated in the summary some of
14 the information relating to potential impacts on
15 children's health, which was discussed also in the SB 25
16 document. So I don't know whether you want to ask any
17 further questions or make any points about this at this
18 point, Paul?

19 --o0o--

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
21 SALMON: Well, I'll proceed to the next one now. The
22 revised summary on acrylonitrile.

23 CHAIRPERSON FROINES: Why did you pick -- why
24 didn't you use 250 instead of 300?

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: I think because typically that -- well, that was
2 the way the -- we normally round these things to one
3 significant figure here. So the 300 is the number. The
4 number didn't, in fact, change substantially from the
5 previous version. Dr. Lewis was responsible for the
6 analysis here, so I want him to respond.

7 STAFF TOXICOLOGIST LEWIS: We had done -- U.S.
8 EPA had done the analysis. They used a BMC10, a ten
9 percent benchmark dose. And their value by using their
10 uncertainty factors was 700 micrograms per cubic meter,
11 very similar to our 800 micrograms per cubic meter.

12 When we initially revised their approach before
13 we had received the original data using a BMC10 and our
14 preferred uncertainty factors, we had a value of 3,000
15 micrograms per cubic meter, so this is slightly lower.

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
17 SALMON: I think the issue which caused us to go back and
18 reevaluate the benchmark was that our preference is to use
19 the BMC05 with our defined range of uncertainty factors.
20 Whereas, the U.S. EPA approach they tend to calculate a
21 BMC10, and then, in fact, put in some additional
22 uncertainty factors, which are not sanctioned by our
23 guidelines, in order to allow for the perception that the
24 BMC10 is, in fact, in effect level rather than being,
25 broadly speaking, equivalent to a NOAEL.

1 So that's the reason for the slight differences
2 in methodology between ourselves and the federal analysis.
3 But, as you can see it comes out basically to
4 approximately the same place in the end, and we feel that
5 the approach we present here is more consistent with our
6 guidelines and with the way we would like to use the BMC
7 calculation methodology.

8 PANEL MEMBER FUCALORO: Just for the arithmetic,
9 can I ask a question? In going from human equivalency
10 concentration of 2.5 parts per million, rather going from
11 6.9 parts per million would be the BMC right, so 2.5 is
12 computationally one half times five-sevenths, essentially,
13 right?

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

16 PANEL MEMBER FUCALORO: And then you bumped it by
17 a factor of 100, and then rounded it off to the next
18 highest? I just want to be clear on that.

19 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
20 SALMON: Yes.

21 PANEL MEMBER FUCALORO: And then you use a 3.1
22 micrograms per cubic meter to get to the conversion factor
23 in order to go from 300 to 800; is that correct?

24 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
25 SALMON: I think actually what we --

1 PANEL MEMBER FUCALORO: That's not quite right.
2 I mean, it should be 900.

3 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
4 SALMON: What we actually do is we go back and we reround
5 the calculation in micrograms per meter cubed, and supply
6 the uncertainties and then do the rounding, so that we
7 don't generate rounding errors.

8 STAFF TOXICOLOGIST LEWIS: Yeah, that's correct.
9 There's no rounding till the end so we had -- it looked
10 like we had 6.86.

11 PANEL MEMBER FUCALORO: Right, I understand.

12 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
13 SALMON: We always do the rounding at the last possible
14 step to avoid generating propagated rounding errors.

15 PANEL MEMBER BLANC: I mean I think it's
16 excellent that you modified the text to be consistent with
17 the evaluations that you did for the childhood project.
18 And on the same vein, do you think it would be useful to
19 insert under a source of exposure as a byproduct of the
20 breakdown of metam sodium in the first pair?

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: Yes, that would be a -- we will do that.

23 PANEL MEMBER BLANC: And do you feel that in the
24 process of the childhood literature review you've
25 basically caught up with all of the recent literature,

1 which this is one of the chemicals of which there tends to
2 be a more evolving literature list there?

3 STAFF TOXICOLOGIST LEWIS: Yes, I think we feel
4 very confident that. We did literature searches as
5 recently as a week or two ago on that on several sources.

6 PANEL MEMBER BLANC: Right.

7 CHAIRPERSON FROINES: Andy, I don't want to get
8 into this right now, but this notion of the BM05 versus
9 BM10, it seems to me that in using a benchmark, one also
10 needs to look at the nature of the data that you're doing
11 the benchmark calculation from, in terms of the degree of
12 extrapolation that you're pursuing.

13 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
14 SALMON: Yes.

15 CHAIRPERSON FROINES: And so it seems to me that
16 one needs to have some flexibility within your guidelines
17 in terms of the data set that's actually used for
18 calculating the benchmark dose.

19 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
20 SALMON: Yes.

21 CHAIRPERSON FROINES: So I wouldn't tie myself so
22 rigidly to a specific value, because you may want to --

23 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
24 SALMON: Well, I think that our philosophy in picking the
25 BMC05, at least when we're reviewing, what I call,

1 "generaltox" animal studies, is that our experience to
2 date has been that the BMC05 has generally been found to
3 have properties fairly similar to the NOAEL, which we're
4 used to dealing with, so that's why we're choosing that.

5 Now, I think it's a very valid point and one
6 which we're struggling with that that may not be suitable.
7 For instance, in some cases we're looking at epidemiology
8 studies, we're particularly depending upon the nature of
9 the endpoint. So, yes, I agree that we need to take
10 everything somewhat on a case-by-case basis. But the BMC
11 is our choice for a starting point at this stage.

12 And the other thing is, of course, that when we
13 are calculating a benchmark, we are using the statistical
14 tools which come in the software to evaluate the quality
15 of it, and, you know, basically to ensure that we are
16 looking at a reasonable data set and not extrapolating too
17 far outside what's defined by the data, so that we do
18 those things.

19 CHAIRPERSON FROINES: I think that's good. I
20 mean, I think that's important, especially when you get
21 into occupational studies at high exposure levels, where
22 obviously you can be in a very different place if you
23 weren't careful.

24 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
25 SALMON: Yes, I think our finding with the benchmark

1 calculation has been that, in general, it's proved a more
2 satisfactory approach to do this calculation than to use
3 the uncertainty factor NOAEL/LOAEL approach, when we don't
4 have a NOAEL -- when we've basically got an unsupported
5 LOAEL, we've often felt ourselves to be rather nervous
6 about, you know, whether the LOAEL uncertainty factor of
7 ten is, you know, appropriate.

8 In some cases it might be too large and in other
9 cases too small. So particularly in that context I think
10 we found the benchmark dose approach to be a more
11 satisfactory way.

12 CHAIRPERSON FROINES: I'm a strong advocate of a
13 benchmark dose approach. I think it's taken too long to
14 be implemented for regulatory purposes. So you don't have
15 an argument from me, but I still would argue that one has
16 to look at the data carefully to make sure one isn't
17 trying to use it when it wouldn't be appropriate.

18 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
19 SALMON: Yes, absolutely.

20 CHAIRPERSON FROINES: Go ahead.

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: So the acrylonitrile, the modifications which
23 were requested by the -- so acrylonitrile REL, we're
24 basically responding to modifications requested by the
25 panel at the last meeting when we considered this, and

1 SALMON: Yes. Basically, we're using the benchmark dose
2 calculation here, which we regard as preferable in this
3 case.

4 And the other consideration which we've added
5 here is the potential for impact on children's health.
6 And there are two pieces of information that we were
7 looking at here. One is that there is a developmental
8 study, and that the chronic REL proposed for this endpoint
9 was significantly lower than the developmental -- than a
10 REL which you would propose on developmental effects.

11 So we feel that the processed REL is likely to be
12 protective against developmental effects and
13 neuro-toxicity again, as I was just saying now. We did
14 look at that endpoint.

15 And although there is an neurotoxic effect from
16 acrylonitrile in adults, this endpoint is less sensitive.
17 And even allowing for the potential increased sensitivity
18 of younger animals or humans to that endpoint, we feel
19 that the proposed chronic REL, which is based on the
20 histology changes in the upper respiratory tract, is
21 likely to be protective of those endpoints for which we
22 have concern as children having differential sensitivity.

23 So that's our proposed analysis on this one.
24 Obviously, we're trying to work within the guidelines that
25 we have put together on this issue, but this is an

1 exploratory exercise, so we very much welcome any input
2 that you have on our approach here, if you think we're
3 doing the right sorts of things and if this is adequate.

4 --o0o--

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

6 SALMON: The next one up is beryllium. We updated the
7 literature review for this analysis. There's been quite a
8 number of things which have come out in the literature
9 since the original version was put together. And in
10 particular three references that Dr. Blanc suggested we
11 should examine more closely have been included.

12 There was also discussion of the uncertainty. In
13 fact, there's an issue here as to -- this is the
14 intraspecies uncertainty factor, and there's a question of
15 whether the responders are a sensitive subpopulation. And
16 if so, whether -- you know, normally we're using a default
17 of ten for this uncertainty factor, but in this case,
18 we're using now an uncertainty of three. We had
19 previously gone all the way down to one, but that was
20 considered illadvised, so we've changed that.

21 Also, we did look for any evidence of
22 differential effects on infants or children. We basically
23 found no indication of any such effects, so we can't
24 really add anything on that, other than to say there's no
25 evidence that there was a problem here. The final thing

1 SALMON: We've been through the arithmetic and found
2 ourselves to be in agreement with the federal axis.

3 PANEL MEMBER FUCALORO: I clearly misunderstood
4 something though. Two slides ago, you talked about a UF
5 sub H from 1 to 3. Now, what uncertainty factor was that?

6 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

7 SALMON: This is for the inhalation.

8 PANEL MEMBER FUCALORO: Got you. This is all
9 right.

10 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

11 SALMON: Apart from that change, the inhalation analysis
12 has not -- you know, is not different than the version
13 that you saw previously. The addition of the oral REL is
14 the thing. And as you see in that case we're not looking
15 at a sensitive subpopulation effect or anything like that,
16 so we're using the standard default uncertainty factors.

17 PANEL MEMBER WITSCHI: I have a comment about
18 your oral data. The effect in the study is they are
19 probably close by the acidity of the beryllium sulfate.
20 And if you go back to the literature on beryllium in the
21 40s and 50s, there are several papers which very
22 conclusively show that beryllium is not absorbed at all
23 into the blood stream from the gastrointestinal tract,
24 because it's precipitated presumably as phosphate. And so
25 this would be mentioned somewhere.

1 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

2 SALMON: Okay. I think that we took note, I think, of
3 your comment previously that the intestinal absorption is
4 low to negligible, but maybe we need to amplify our
5 language a little bit to make it clear that we're aware of
6 that, and so we will do that.

7 Yes, I mean, it's a slightly curious situation,
8 but, you know, there's a pathological endpoint here by the
9 oral route, so we feel obliged to respond to it at some
10 level.

11 PANEL MEMBER BLANC: Yeah. I mean the issue here
12 is that the significance of oral exposure, even without
13 systemic absorption is the same issue as the effect of
14 skin contamination through airborne sources, which would
15 tend to potentially sensitize someone as well. So if you
16 sensitize someone through oral route, and then have them
17 exposed by inhalation, they'd be, well, theoretically,
18 particularly more likely to respond to the beryllium that
19 they inhaled.

20 So for that reason, the oral exposure would be
21 meaningful as nerve sensitization viewed without any
22 absorption. The implication is not that you're absorbing
23 beryllium systemically and then depositing it
24 preferentially in the lung, but rather that you're
25 becoming sensitized theoretically, I guess, through some

1 oral contamination. It's, I think, much more likely you
2 become sensitized through skin contact and then because
3 you're systemically sensitized, once you inhale it, you've
4 developed chronic beryllium disease.

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
6 SALMON: It would be nice if we had experimental data that
7 would enable us to analyze that kind of situation more
8 fully, but unfortunately, you know, what you see is what
9 we can find in the literature here. So we hope that we've
10 addressed those issues in some way at least with the
11 approach we're taking here.

12 PANEL MEMBER BLANC: Well, since you don't take
13 into account the skin route, it doesn't bother me that you
14 have the oral thing in there, because one probably
15 counter-balances the other, even if it's, you know, overly
16 conservative having the added oral burden that you can't
17 real calculate the skin content burden.

18 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
19 SALMON: Yeah, that's right, we don't have a good way of
20 dealing with that, at this point, so this is hopefully
21 providing sufficient protection.

22 Thank you.

23 --o0o--

24 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
25 SALMON: The next one I want to present is the

1 fairly low number reflective of the fact that there is a
2 high irritant material.

3 --o0o--

4 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

5 SALMON: When we looked at the children's health issue,
6 we're conscious of the fact that this endpoint is
7 potentially one which does have a differential impact on
8 infants and children. The finding has generally been that
9 irritants do exacerbate asthma at least in people already
10 suffering from asthma.

11 There is some suggestion that actually induction
12 of asthma or insensitive subjects including people who are
13 atopic may also occur. But there, as you heard earlier,
14 in the SB 25 discussions, there's a number of
15 uncertainties about exactly what is going on here,
16 particularly with agents like chloropicrin, which,
17 frankly, there have simply not been studies with respect
18 to this sort of consideration.

19 It's fairly easy to see why people have not done
20 those response studies with chloropicrin on children. But
21 nonetheless, from the point of view of undertaking this
22 analysis, it represents a serious data gap. We are unable
23 to point to any specific indications that the methodology
24 is inadequate.

25 In particular, we do have the intraspecies

1 uncertainty factor of ten included in the calculation,
2 which we believe, by default, allows for the existence of
3 sensitive subpopulations within the general human
4 population. And in particular we think that children, and
5 especially asthmatic children, might be such a sensitive
6 subpopulation.

7 So we're basically relying on the existing
8 uncertainty factor of ten to accommodate that hypothesized
9 sensitive subpopulation. We don't have any specific
10 evidence or guidance, at this point, which would encourage
11 us to do anything other than that, so this is what we're
12 proposing.

13 CHAIRPERSON FROINES: One could argue that if one
14 looks at the history dating back to the 1950s of risk
15 assessment approaches, and the development of the
16 uncertainty factor, safety factor approach, one would
17 argue that the definition of the safety factor for
18 intraspecies variability was never intended as a
19 historical matter to address differences in adult versus
20 children sensitivity.

21 And that there's no, sort of, underlying
22 intellectual basis to make that assumption, so that it's
23 something that I think needs to be reviewed as we move
24 forward, because, in a sense, what you say is that we have
25 a safety factor of ten and we assume that it includes

1 within the distribution children, but that's not
2 necessarily an assumption that has an underlying basis to
3 it. It's an add-on almost.

4 And I think that that's probably an inadequate
5 way of looking at it. If you were writing it -- instead
6 of putting up a set of numbers, if you were writing it in
7 some sort of intellectual context, I don't think you would
8 feel quite happy with that formulation, frankly.

9 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

10 SALMON: I agree. And obviously, this is an area where we
11 are going to have to put in additional work. We have a
12 mandate under the SB 25 program to develop improved risk
13 assessment guidelines for specifically taking into account
14 effects on infants and children. And this is clearly one
15 of the areas where such development is needed.

16 I think the situation we have at the moment is
17 that we are lacking in either a default guidance, other
18 than we're sort of vaguely trying to adapt to the purpose
19 here. And we don't have any specific data on
20 chloropicrin. I think what we hope is that in the long
21 term, we may be able to identify cases where there are
22 sufficient data that we can perhaps come up with something
23 more satisfying as a general guideline and will then be
24 able to extrapolate that to other chemicals like
25 chloropicrins, which we don't have the data.

1 And, of course, if during that process we
2 identify something which says that we're not right in
3 making this default assumption here, then we would have
4 to, by definition, that would immediately identify any
5 chemicals where we had made the assumption as chemicals
6 which should be added to the list of critical materials
7 for reevaluation, bearing in mind that we have a program
8 for checking into and prioritizing all the toxic air
9 contaminants. And we actually have to have reevaluated
10 another ten by 2004.

11 CHAIRPERSON FROINES: I just think as a general
12 matter and we have to move on because we have a lot to
13 cover that's important, but I don't think that population
14 heterogeneity, which brings about the safety factor of
15 ten, really includes variations in children's exposure
16 physiology, so on and so forth.

17 And so that, in a sense, it's broadening the
18 distribution, and therefore assuming a factor of ten is
19 okay, and I suspect that it may not be.

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
21 SALMON: If you can, you know, point us in a direction
22 where we should go, at this point, with this REL, I think
23 we'd be very happy.

24 CHAIRPERSON FROINES: Yeah, I agree. I think
25 with this REL it's impossible, but even in terms of the

1 general premise, it's obviously a difficult one.

2 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

3 SALMON: Yes, we're at a preliminary stage.

4 --o0o--

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

6 SALMON: The next one is --

7 PANEL MEMBER BLANC: One very small question just

8 on the -- this is a methodologic issue in terms of how you

9 handle these in general.

10 But on this particular chemical for the physical

11 properties when you get to the vapor pressure, you site a

12 reference for the vapor pressure, and it's a 1921

13 reference, which is pretty long ago. You don't generally

14 site, parenthetically, the reference source for vapor

15 pressure in the introductions.

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

17 SALMON: I think --

18 PANEL MEMBER BLANC: And is that because you just

19 couldn't confirm the vapor pressure from any other more

20 recent source?

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: I think what happened here was that, I suspect,

23 working from slightly different reference sources than

24 this one, that we generally, use this, obviously is a

25 slightly unusual chemical, and it has considerable

1 pesticidal uses and things of that sort.

2 And also --

3 PANEL MEMBER BLANC: It gives the impression
4 of -- anachronism isn't the right word, but you know one
5 would --

6 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
7 SALMON: Yes. In this particular case, the reference is
8 from a treatise on chemical warfare.

9 PANEL MEMBER BLANC: I understand that.

10 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
11 SALMON: I suspect this is reflective of the unusual
12 nature and terms and reference to the compound.

13 PANEL MEMBER BLANC: Yeah, but you should be able
14 to find it in the MERCK Manual, too, I would think.

15 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
16 SALMON: We have been enjoined to use primary references
17 where they're available. But maybe a more up-to-date
18 reference, if we can find one, would be right.

19 CHAIRPERSON FROINES: Well, I think that the
20 answer to the question would be to write the manufacturer
21 of chloropicrin to the degree that anybody is making it.

22 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
23 SALMON: Well, we could probably obtain a more recent
24 statement through the Department of Pesticide Regulation.

25 PANEL MEMBER BLANC: Yes. And I assume that the

1 key papers that you have used that we're exposing animals
2 through generating saturated vapors of this solution must
3 have stated what the vapor pressure was?

4 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

5 SALMON: Yes. Well, they probably cited this reference.

6 PANEL MEMBER BLANC: That's how you got to it in
7 the first place?

8 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

9 SALMON: Yes, I think probably it is.

10 Diethanolamine, again, we are responding to early
11 comments by the panel, and also including consideration of
12 children's health impacts. And there's a change in the
13 critical study and endpoint. This new study is one which
14 was actually submitted to us. It's basically a regulatory
15 type study that was done more recently than the one that
16 we previously had access to.

17 But it's not especially remarkable in other
18 respects, but it is a newer and more comprehensive study
19 than the one that we were using previously.

20 And so it's a chronic inhalation study, and we're
21 using a NOAEL/LOAEL approach here. My sense is that we
22 were looking -- we looked at the data table in the
23 analysis. In fact, we haven't got a data set here for
24 which we can use the benchmark dose methodology, because
25 we've got basically close to 100 percent response in some

1 of the -- well, in fact, in virtually all of the
2 categories, so we were not able to get a statistically
3 acceptable analysis using the benchmark dose approach. So
4 this one we're staying with the NOAEL/LOAEL methodology.

5 --o0o--

6 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

7 SALMON: And so the LOAEL uncertainty factor we chose was
8 an uncertainty factor of three based on the nature of the
9 effect, which was the hyperplasia and metaplasia were in
10 the larynx were in an extremely localized area. And the
11 rest of the respiratory tract didn't show any changes
12 until higher doses.

13 So we felt justified in arguing that this was a
14 less severe effect than the more widespread irritation and
15 pathological changes which we've chosen to regard as a
16 critical effect in some other studies.

17 So we then applied the usual approach of
18 uncertainty factors.

19 --o0o--

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

21 SALMON: Subchronic uncertainty factor of three relates to
22 the duration of the study which is a 90-day study. And,
23 in fact, we come up eventually with a cumulative
24 uncertainty factor of 1,000, which is, you know, the
25 highest that we normally consider.

1 The proposed chronic REL based on the upper
2 respiratory tract effects is considerably lower than the
3 comparison REL, which was based on fetotoxicity. So from
4 the point of view of any developmental effects, we see
5 this proposed REL as protective of infants and children.

6 Again, we're seeing it is a respiratory irritant
7 which might exacerbate asthma, and have, thereby, an
8 adverse effect specifically on some children.

9 However, we felt that in this case the inclusion
10 of the overall uncertainty factor of 1,000 would probably
11 be sufficient to reassure us that we were okay with the
12 proposed REL in the situation where there's no direct
13 evidence that diethanolamine exacerbates asthma or would
14 allow us to quantify any other means for differential
15 impact on infants and children.

16 PANEL MEMBER BLANC: Although, there are case
17 reports of allergic sensitization of asthma by
18 diethanolamine, aren't there not? This is not an irritant
19 just as this would, sort of, be presumably.

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
21 SALMON: I don't know that we have any quantitative
22 information about exposure that would allow us to use
23 those.

24 PANEL MEMBER BLANC: You probably wouldn't.
25 There would just be --

1 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

2 SALMON: This is a recurrent problem with this sort of
3 report, that, you know, it's something which may be out
4 there but we don't know.

5 PANEL MEMBER BLANC: Well, you would have it to
6 the extent that if it was one of the cases where someone
7 did a specific inhalation challenge to document that
8 causal relationship, then you would.

9 STAFF TOXICOLOGIST LEWIS: We did list one case
10 report of a person occupationally exposed to
11 diethanolamine with occupational asthma.

12 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

13 SALMON: I think the situation here --

14 PANEL MEMBER BLANC: Which reference is that?

15 CHAIRPERSON FROINES: Page A 28. It's under 4
16 Roman Numeral 4 on A 28.

17 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

18 SALMON: Some of these in occupational studies are a
19 little bit retro in terms of the methodology and
20 conditions.

21 PANEL MEMBER BLANC: And when you pulled that
22 case report, had they done an inhalation challenge, do you
23 know?

24 STAFF TOXICOLOGIST LEWIS: I didn't see the
25 report myself.

1 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

2 SALMON: I don't believe they did. No, I think it is
3 literally just a case report.

4 PANEL MEMBER BLANC: You might just double check
5 that, because that would give you at least that exposure
6 level that would trigger a response in someone who's been
7 sensitized. I'm not familiar with the case report, so I
8 can't tell you.

9 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

10 SALMON: I think, but we'll check into it anyway.

11 PANEL MEMBER BLANC: Now, sometimes it's so crude
12 that it's only to have him go into the workplace and then
13 they prove that he has dropped his FEV1, but sometimes
14 it's a control exposure, and they would actually have a
15 concentration level that you could cite.

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

17 SALMON: We'll make sure that there isn't -- when we can
18 have another look for that, but at this point --

19 PANEL MEMBER BLANC: I don't think it would
20 change anything else you've done. It would be just good
21 for your documentation.

22 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

23 SALMON: We would want to know. So we'll have another
24 look and see if we can find anything.

25 PANEL MEMBER BLANC: In that particular paper,

1 yeah.

2 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

3 SALMON: Right.

4 CHAIRPERSON FROINES: The interesting thing about
5 this compound is that given the toxicologic data that you
6 site, it has interesting implications for occupational
7 exposures.

8 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

9 SALMON: Um-hmm.

10 The level that we came up with was quite a bit
11 lower than I think the -- you know, we received this study
12 as part of a public comment, basically. And I think they
13 were expecting us to come up with an evaluation which was
14 rather less stringent than the one that we actually
15 produced. I'm not quite sure why they had that
16 expectation, but it may have something to do with their
17 perception of how the material was seen in terms of
18 occupational health at the present time.

19 --o0o--

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

21 SALMON: The next one I'd like to present is ethylene
22 dibromide. And this is one which we came up with the
23 analysis in March, but I think is a -- I think I'm correct
24 in thinking that this is one of the ones that Dr. Friedman
25 was in charge of, and he wasn't at that meeting, so we

1 developmental toxicity endpoints in rodents. And we
2 actually include an analysis of this in the summary for
3 comparison, I think, which you -- anyway, basically the
4 fetotoxicity in rodents was reported at significantly
5 higher levels.

6 So we're thinking that the proposed REL should be
7 adequately protected against those developmental effects.
8 We have no direct evidence that the reproductive toxicity
9 endpoints in humans would have a differential impact on
10 infants and children, although it's possible,
11 hypothesizing that adolescent boys might be more sensitive
12 than adults then.

13 Given that metabolism is an important factor in
14 the toxicity of this compound, there's a possibility that
15 there might be metabolic differences between infants,
16 children and adults. We don't have any evidence about
17 this. So again, I think we're in a situation of wanting
18 to put, if you like, put a thumb print on this as
19 something that we should continue to look at carefully.
20 But for the time being we are really stuck with, assuming
21 that our regular methodology is sufficiently cautious, to
22 protect the infants, children and adolescents as well as
23 the adults.

24 PANEL MEMBER FRIEDMAN: Can I ask you about a
25 different metabolic capability in children versus adults,

1 is there a certain direction that you would expect or
2 could it go both ways, one they could metabolize it better
3 or worse?

4 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

5 SALMON: What we've seen so far, is that things can change
6 in both directions. Typically the -- well, the
7 differences from what you would call sort of childhood
8 throughout adolescence and adulthood are typically not
9 very large, but what you do see is quite significant
10 changes between fetus, newborn and infant, you know,
11 during that phase, there are changes.

12 And a lot of enzymes in the fetus are, you know,
13 for instance, the cytochrome B450 enzymes are different.
14 And the absolute level of their activity is often somewhat
15 lower by the standard assays, but we often, in fact, see
16 higher sensitivity in the fetus and the infant in spite of
17 having lower activity of Phase 1 enzymes, because the
18 activity of the Phase 2 enzymes is often lower, too, and
19 obviously the toxicological outcome depends on the balance
20 between the Phase 1 and the Phase 2 enzymes.

21 And in some cases the Phase 2 enzymes are more
22 depressed in the infant or fetus than are the Phase 1
23 enzymes. So the answer is it can go either way in terms
24 of the outcome.

25 PANEL MEMBER FRIEDMAN: And what is Phase 1 and

1 Phase 2 mean?

2 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

3 SALMON: Phase 1 is the activating enzymes that typically
4 the oxidative actions of cytochrome P450s is sort of the
5 classical example, which is the thing which actually
6 generates reactive intermediates, such as epoxies or
7 things of that sort.

8 And the Phase 2 is the detoxifying enzymes,
9 typically glutathione transferases, and ultratransferases,
10 things of that sort.

11 CHAIRPERSON FROINES: Andy, I'm very concerned
12 about this 2:00 o'clock cutoff that we have, and so I'm
13 going to have you go till 11:30. I'm very anxious to have
14 the pesticide discussion today and the findings for SB 25.
15 So I'm going to go till 11:30 with your presentation, then
16 I'm going to cut it off and move on the agenda, and then
17 we'll come back to anything we haven't finished as we get
18 finished with the other two.

19 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

20 SALMON: Do you want me to try and --

21 CHAIRPERSON FROINES: So we should try and push
22 ahead, you know, spending a lot of time on EDB is a
23 exercise in futility, given how much, how little is used
24 in the environment in California.

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: Well, if there are any comments or suggestions or
2 additions that the panel wants to send us, obviously we'd
3 be happy to deal with them.

4 --o0o--

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

6 SALMON: The next one to look at is isophorone. The panel
7 has reviewed the REL development for this compound in
8 March. We're bringing it back to you here because we've
9 added a section on differential impacts on children's
10 health.

11 And in this particular case the REL is based on a
12 developmental study. And we feel it's therefore
13 reasonable to expect that it should be adequately
14 protective of infants and children. However, there is no
15 direct evidence in the literature that would quantify any
16 differential effects of isophorone in children relative to
17 adults.

18 So apart from this conclusion that since we're
19 using developmental endpoints as the critical endpoint and
20 that that's the basis of the REL, really we don't have
21 anything else to add and we haven't otherwise changed the
22 analysis significantly from when you last saw it.

23 So if this is seen as a reasonable response to
24 the data from the point of view of considering the impacts
25 on children's health, then this is it.

1 PANEL MEMBER BLANC: Given your allusion to
2 children's health and given the aside that this chemical
3 occurs naturally in cranberries, and given the fact that
4 children's intake of juice per kilogram is rather high, do
5 you need to include one of your orals or is it such a
6 trace trivial?

7 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
8 SALMON: I think it's a relatively minor component. I
9 don't, of course at this point, have an analysis for you
10 on oral toxicity specifically. We don't have a mandate to
11 consider food and constituents under the hot spots
12 program. And I don't think that this qualifies as
13 multi-media. So in this particular context, we don't have
14 much of a handle on that issue, but it may well be that
15 although this -- let me get to the right data here.

16 We don't have a particular reason for including
17 oral isophorone at this point, and for the hot spots
18 purpose, but it may well be relevant certainly in more
19 general terms in consideration of children's health.

20 PANEL MEMBER BLANC: Okay.

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
22 SALMON: I think, I mean the question of oral exposures
23 and sensitivity of children is clearly an important one
24 with implications for our overall consideration of how we
25 think about children's health impacts. And isophorone is

1 majority of the population.

2 --o0o--

3 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

4 SALMON: The next one -- I'm looking at the time here, I
5 hope I'm not rushing you too much here.

6 The next one I want to present is methyl
7 isocyanate, and the changes are quite limited. One of the
8 things that the panel asked us to do, the earlier review,
9 was to actually include some data on the amount or some
10 indication of the amount that might be involved as a
11 breakdown product from metam sodium use. It has been
12 identified as a minor breakdown product in the environment
13 after metam sodium use.

14 And this, in fact, looks as if it might be by a
15 significant margin the largest single source of the
16 material, at least in the Californian environment and
17 possibly apart from a couple of specific industrial hot
18 spots. So this is a value.

19 We don't have a number for the amount of methyl
20 isocyanate that might be involved, but we do have a number
21 of metam sodium used and it clearly is fairly
22 considerable. This is an average over the years of '95 to
23 '99.

24 The other issue is the differential impacts on
25 children's health. We do have a reproductive study which

1 did not identify any increased sensitivity of the fetus
2 relative to the parent. So we're thinking that, at least
3 from that point of view, the chronic REL should be
4 protective of infants and children.

5 Again, we have this concern that because it's a
6 severe respiratory irritant, there may be a variety of
7 different impacts on infants and children. And the fact
8 of the matter is we don't have a direct quantitative
9 indication of what that might be. So, again, we are
10 having to rely on the defaults on intraspecies uncertainty
11 factors at this point.

12 PANEL MEMBER FUCALORO: Can I ask you a quick
13 question on the major uses and sources, maybe you
14 mentioned this before. Based on the most recent
15 inventory, the annual statewide industrial emissions from
16 facilities reporting under the toxics air hot spots at
17 California estuaries to be .29 pounds.

18 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
19 SALMON: Yeah.

20 PANEL MEMBER FUCALORO: That's it. .29 pounds.

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: The major --

23 PANEL MEMBER FUCALORO: I know the major isn't
24 the metam sodium, but --

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: I mean, obviously this material is used in
2 various kinds of industrial processes, but it appears that
3 those industrial processes are not ones which typically
4 are carried out in California. So our concern --

5 PANEL MEMBER FUCALORO: .29 pounds, they'd even
6 report that.

7 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

8 SALMON: Yes.

9 PANEL MEMBER FUCALORO: I mean, are you sure the
10 number is right?

11 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

12 SALMON: Let's say I have as much confidence in that as in
13 the other numbers we've pulled off the hot spots data.

14 PANEL MEMBER FUCALORO: No, no, seriously, is
15 there not a typo or something?

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

17 SALMON: I don't think so.

18 CHAIRPERSON FROINES: It's clearly wrong. We
19 should check it. It's years old.

20 PANEL MEMBER FUCALORO: You may be wrong in terms
21 of not --

22 CHAIRPERSON FROINES: A lot of the data that gets
23 cited under the toxic hot spots is really one wouldn't
24 want to bet one's life on by any means. So I think that I
25 always just take it with a grain of salt and go on and

1 don't take it seriously for the most part.

2 Unfortunately, that's the state of that data and
3 we probably should talk about it sometime in another
4 meeting where we go back and look and see how dated that
5 information is and really how much confidence one can put
6 to it, because it ends up in all these documents as though
7 those are realistic figures and they're not.

8 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

9 SALMON: Well, it's obvious that any reporting under that
10 hot spots database is somewhat constrained by who chooses
11 to report.

12 PANEL MEMBER FUCALORO: I guess I'm asking -- I
13 mean, I don't want to belabor the point, but the hot spots
14 reported as, estimated as -- I mean, you actually have a
15 list of things that are saying that this toxic thing was
16 under a pound a year in all of California.

17 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

18 SALMON: That's the numbers we came up with.

19 PANEL MEMBER FUCALORO: That's the numbers you
20 see.

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: Whether it's right, we need to check.

23 PANEL MEMBER FUCALORO: I can understand
24 something like a dioxin, but I mean this is something --

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: We'll check into that and make sure there isn't

2 --

3 CHAIRPERSON FROINES: I think that the selection
4 of values all have a certain ridicule value associated
5 with them. And when you put something into a document
6 that has a super high ridicule value, that's probably been
7 a bad judgment.

8 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

9 SALMON: You feel we should simply delete that.

10 CHAIRPERSON FROINES: I would not -- yeah, I
11 would.

12 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

13 SALMON: We can do that if you think that's appropriate.

14 CHAIRPERSON FROINES: .29 pounds?

15 PANEL MEMBER FUCALORO: First check it.

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

17 SALMON: Yes. Well, we'll check it and if we're not happy
18 with what we find, we'll --

19 PANEL MEMBER BLANC: Well, the simple solution
20 would simply be, the remainder of the sentence after it
21 says "...in California were negligible."

22 PANEL MEMBER FUCALORO: And the metam sodium was
23 not.

24 PANEL MEMBER BLANC: They're not reporting
25 anything other than that.

1 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

2 SALMON: I think that's probably the most accurate way and
3 diplomatic way of characterizing it, so we'll do that.

4 PANEL MEMBER BLANC: What you expect, because
5 nobody uses those chemicals as a direct intermediate, it's
6 an unanticipated byproduct by and large except in very,
7 very limited -- I think it's Hopewell, West Virginia is
8 the only place in the United State where it's used
9 regularly as a chemical.

10 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

11 SALMON: Well, nobody is making a carbaryl in California.

12 PANEL MEMBER BLANC: So nobody should be
13 reporting release of it.

14 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

15 SALMON: Yeah.

16 PANEL MEMBER BLANC: In fact, if anybody reported
17 any release of it, it would make you wonder what they were
18 doing.

19 (Laughter.)

20 CHAIRPERSON FROINES: But I think, at some point,
21 at a meeting in the future, it would be worthwhile to have
22 a discussion about the hot spots program, because we
23 haven't had one in years and years and years, and it would
24 be very useful to discuss the validity of the data that's
25 currently in the hot spots program, because I won't go

1 into more detail, but my understanding of the program is
2 that it's been on hard times. And so it's something that
3 would be good for this panel to be aware since we have --
4 since every chemical that we get has a value essentially
5 from the hot spots program or very many.

6 And it would be useful to have a sense of how do
7 we view that information. And I look back and Lynn's
8 nodding his head and George is nodding his head, so I feel
9 comfortable saying that.

10 But I think this is an area that's somewhat
11 problematic, because our information on exposures tends to
12 be a limiting factor in some respects.

13 Now, as a related question, and Lyn Baker may
14 have an answer, which is it would be useful to know
15 something about what kinds of exposures are occurring to
16 MIC. And it's my understanding that whereas there has
17 been some studies of MITC, I don't know if there has been
18 any attempt to quantify MIC. Is there a comment, because
19 I think that's a -- obviously, given the sensitivity of
20 MIC because of Bhopal, it's not a trivial issue,
21 potentially anyway.

22 MR. BAKER: Hi, Dr. Froines. Lynn Baker from the
23 Air Resources Board. I can address that briefly. We did
24 do some MITC monitoring a couple of years ago around a
25 specific application, and we did do monitoring also for

1 MIC, but that was just a short-term study.

2 However, this year, we did do eight weeks of
3 monitoring in Kern County for both MITC and MIC, so
4 ambient monitoring, which we don't have the data yet, but
5 early next year we will have that data available.

6 CHAIRPERSON FROINES: Well, that will be
7 interesting to come back to, given the 15 million pounds
8 currently in use, to see what it looks like.

9 Thanks Lynn.

10 And, Andy, one final question, at Bhopal do you
11 have any sense, and I realize this is a very poor
12 question, but was there any indication that children were
13 differentially affected?

14 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
15 SALMON: Not --

16 CHAIRPERSON FROINES: I mean clearly there was
17 such a horrendous event that it's hard to ask that
18 question.

19 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
20 SALMON: Not that I'm aware of in terms of the acute
21 effects. There were reports of some adverse reproductive
22 and developmental outcomes, which would come within the
23 purview of our consideration here, but those are hard to
24 quantify, because of the -- among other things, because of
25 the difficulty of collecting data in that population. In

1 fact, they have a fairly high level of disease related
2 reproductive problems in the population already.

3 So that's a little bit of a gray area. But it's
4 my belief that there are some reports of developmental
5 issues following the Bhopal accident, but nothing
6 specifically to say that the acute damage to the eye or
7 the lung was particularly severe in children.

8 CHAIRPERSON FROINES: Thanks. I think we'll call
9 a quit for a moment, hopefully getting back to it, if
10 that's okay.

11 Does the panel want to take a five minute break
12 so the court reporter can take a break?

13 Then we'll talk about the SB 25 findings.

14 (Thereupon a recess was taken.)

15 CHAIRPERSON FROINES: The next item on the Agenda
16 is going to be the panel consideration of the findings of
17 our deliberations based on SB 25.

18 You have an updated version of the document,
19 which is most of the changes that have been put in are
20 small and editorial in nature. There is one major change
21 which I'll call your attention to that we thought was
22 important under Section 15 on pesticides.

23 We've added a sentence, it's on page 615, and it
24 states as follows, "In the toxic air contaminant program,
25 there is" -- this is not, perhaps, written -- "there is a

1 parallel program where the Department of Pesticide
2 Regulations identifies pesticides as Toxic Air
3 Contaminants. The panel recommends that parallel or
4 similar consideration of children be given in the
5 evaluation of pesticides and their pesticidal use."

6 The intent of that sentence is to say that the
7 decision to leave pesticides out of SB 25 needs to be
8 reconsidered in the future, so that we can have inclusion
9 of pesticides as well as other chemicals. And that's the
10 purpose of that sentence, and that's consistent with the
11 dialogue that occurred over the four meetings that we had
12 on SB 25 where there was continually stated concern about
13 the absence of pesticides. And so that's the one
14 difference that you have over the draft that you've
15 already seen.

16 So we need to decide whether this draft is
17 satisfactory and whether we can send the findings forward.
18 So I guess the best way to do that is to ask each
19 individual for comments. We have comments from Stan
20 Glantz who said that he thought that the document was
21 fine, except we needed to make changes where we change
22 PAHs to POMs to be consistent with the TAC listing, and so
23 we've made those changes and you can see that in the text
24 that you're currently looking at.

25 So why don't we proceed.

1 PANEL MEMBER BLANC: Can I just ask one
2 clarification. The way you have the arrows drawn for that
3 final -- for what would then become the next to last
4 statement regarding methyl bromide, "one exception is
5 methyl bromide noted in finding 13 above." And you have
6 this little arrow suggesting that you're going to move
7 that to proceed the sentence, "However SB 25 reiterated
8 and confirmed by statutory," you were going to move that
9 before that? That's the way I would interpret that arrow.

10 CHAIRPERSON FROINES: That was what we thought
11 would work.

12 PANEL MEMBER BLANC: I would leave it where it
13 is.

14 CHAIRPERSON FROINES: Where it is, okay, and put
15 the other in between.

16 PANEL MEMBER BLANC: And you were proposing to
17 put the other at the very end and I think that's fine
18 where you have it. I just wouldn't -- it doesn't make
19 logical sense to put the methyl bromide sentence, but I
20 think ending with the sentence that you propose which is,
21 "In the air contaminant program, there is a parallel
22 program in which the Department of Pesticide Regulation
23 identifies pesticides as Toxic Air Contaminants. The
24 panel recommends that parallel or similar considerations
25 of children be given in the evaluation of pesticides in

1 their pesticidal use" is fine as the final two sentences.

2 CHAIRPERSON FROINES: So do you have other
3 comments, Paul?

4 Why don't we go to you first.

5 PANEL MEMBER BLANC: I don't have any problems.
6 I think the version, as proposed, reflects the previous
7 discussion.

8 CHAIRPERSON FROINES: Roger.

9 PANEL MEMBER ATKINSON: No, I don't have any
10 comments.

11 CHAIRPERSON FROINES: Gary.

12 PANEL MEMBER FRIEDMAN: I thought it was fine. I
13 just would like to ask for clarification of the
14 handwritten item at the end of number six, I can't read
15 the last part of it, "add sentence, health effects
16 discussed." Is it --

17 DR. FANNING: Maybe I can address that.

18 Ellinor Fanning.

19 PANEL MEMBER BLANC: Can you just read it to
20 start with?

21 DR. FANNING: The language isn't set yet, but it
22 says here, "Health effects discussed are those pertinent
23 to SB 25 and not necessarily all health effects associated
24 with a specific substance."

25 So the idea being that your findings that a

1 particular compound should be listed as a high priority
2 for children's health may not fully articulate all the
3 important health effects that that compound has, but will
4 really focus on the ones that you used in your
5 deliberations to select that compound.

6 CHAIRPERSON FROINES: Let me give you an example
7 of what's meant there. In the decision to list diesel,
8 for example, emphasized asthma, the adjuvant effects of
9 asthma, the enhancing effects of diesel on asthma. And so
10 the basis for the listing of diesel was a noncarcinogen
11 respiratory endpoint.

12 However, we also know that this panel has found
13 diesel as a carcinogen in the past and so that -- but that
14 was not the basis of identifying diesel within the SB 25
15 context. But we wanted to call attention to the fact that
16 there are other health endpoints that are not necessarily
17 listed that may have consequences beyond their -- beyond
18 the differential toxicity criteria.

19 PANEL MEMBER FRIEDMAN: I wonder if it wouldn't
20 be worthwhile giving an example here like that because
21 otherwise it's sort of unclear as to what you're talking
22 about, whereas when you discussed that diesel example just
23 now, it became very clear to me what you were talking
24 about.

25 CHAIRPERSON FROINES: Okay.

1 PANEL MEMBER FRIEDMAN: I don't know if the
2 others feel that this is clear what you mean and the other
3 readers will know it's clear, then I don't feel strongly
4 about that. To me, it would help to give an example like
5 that.

6 CHAIRPERSON FROINES: Does everybody agree?

7 PANEL MEMBER BLANC: Do you mean -- when you say
8 specific example, do you mean generically adult
9 carcinogenicity or do you mean carcinogenesis due to
10 diesel associated with diesel exposure?

11 PANEL MEMBER FRIEDMAN: Something like that.

12 PANEL MEMBER BLANC: So you mean specifically
13 with a specific chemical citation?

14 PANEL MEMBER FRIEDMAN: Right, right.

15 PANEL MEMBER BLANC: I would actually recommend a
16 middle ground where we simply said carcinogenesis in
17 adults without going into -- because it would unduly
18 weight it if we cite one chemical and we're not citing
19 another one.

20 PANEL MEMBER FRIEDMAN: That would be fine. I
21 would accept that.

22 PANEL MEMBER BLANC: Let me propose the precise
23 language, since I think the record really needs to reflect
24 what the precise sentence is we're adding. And therefore
25 reading Ellinor's writing, I would say -- and putting in

1 the missing words, the sentence would be, "The health
2 effects discussed are those pertinent to SB 25 and not
3 necessarily all of the health effects associated with each
4 specific chemical, for example, adult carcinogenesis."

5 PANEL MEMBER FRIEDMAN: That would be fine. I
6 don't know if you need the word specific in there, just
7 each chemical.

8 PANEL MEMBER BLANC: Fine, delete the word
9 specific.

10 CHAIRPERSON FROINES: Gary, are you done?

11 PANEL MEMBER FRIEDMAN: Yes, sorry. No, I was
12 happy with it except just clarifying that.

13 CHAIRPERSON FROINES: But you have no further
14 comments.

15 PANEL MEMBER FRIEDMAN: Right.

16 CHAIRPERSON FROINES: Tony.

17 PANEL MEMBER FUCALORO: Under number 5, the
18 second sentence says, "Available data on ambient air
19 concentrations and health assessment values, including
20 Reference Exposure Levels and Unit Risk Factors, were
21 gathered for all TACs and used for a screening level risk
22 ranking."

23 Now, that's a jumble of gerrands, participles and
24 nouns used as adjectives, and I'm not sure I know what it
25 means, so I think perhaps a clarification of that is

1 suggested.

2 Down several lines --

3 CHAIRPERSON FROINES: Wait, wait. Let's finish
4 each thing before we go forward, because then we'll be
5 finished with the document and we can go.

6 PANEL MEMBER BLANC: I would suggest the
7 following change then to finish the sentence "...were
8 gathered for all TACs and used for ranking risks at a
9 screening level."

10 PANEL MEMBER FUCALORO: Yes. Then several lines
11 down it says, "From the 37 compounds for which literature
12 reviews were developed OEHHA and this panel identified 17
13 TACs..." Is that accurate?

14 CHAIRPERSON FROINES: No.

15 PANEL MEMBER FUCALORO: Was it not just OEHHA who
16 did it?

17 CHAIRPERSON FROINES: Yes. Well, no not
18 entirely.

19 DR. FANNING: Well, actually that was intended to
20 reflect the discussion where originally there were 11 on a
21 list that OEHHA had brought to you. And the panel did act
22 to add five or six more, I can't remember the numbers at
23 this point, to that list. So perhaps it's not quite
24 correct to say you both identified that.

25 PANEL MEMBER BLANC: I would say "...OEHHA,

1 responding to panel feedback..."

2 DR. FANNING: Okay.

3 CHAIRPERSON FROINES: Yeah, I think it's better
4 for us not to -- we don't identify things.

5 PANEL MEMBER FUCALORO: I was concerned about
6 that.

7 And this is my last one, this is a typo, it's
8 very easy. The last sentence in that, it seems to be all
9 in here, it's not the only one I read, but it's the only I
10 have comments about. "Thus extensive exposure was a key
11 criterion..." rather than "an key criterion." Just a
12 typo.

13 That's all.

14 CHAIRPERSON FROINES: That shows that you were
15 thorough, however, when you changed "ands" to "As", so we
16 give you a gold star.

17 PANEL MEMBER BLANC: That means he has a good
18 liberal arts education.

19 (Laughter.)

20 PANEL MEMBER FUCALORO: I didn't have one, I'm
21 just teaching liberal.

22 CHAIRPERSON FROINES: Peter.

23 PANEL MEMBER WITSCHI: Yeah, I would say I'm very
24 happy with the table on page five. I have a small
25 suggestion since we identified benzene and vinyl chloride

1 as new carcinogens. We might as well also define arsenic
2 as a human carcinogen.

3 What's the status of formaldehyde, by the way?

4 CHAIRPERSON FROINES: I don't think -- I think
5 it's still probable.

6 PANEL MEMBER WITSCHI: It's still probable.

7 CHAIRPERSON FROINES: I believe it's still a 2A.

8 PANEL MEMBER WITSCHI: That's fine, but we
9 definitely should identify arsenic as a known one. But I
10 think this table is very well done. It reflects my
11 concern I had with the longer descriptions quite well.

12 CHAIRPERSON FROINES: Yeah, I think the table
13 really is a major improvement.

14 PANEL MEMBER FUCALORO: It was very helpful.

15 CHAIRPERSON FROINES: Craig.

16 PANEL MEMBER BYUS: Yeah, I was quite pleased. I
17 think it was very nice findings considering the difficulty
18 we had, a lot of the deliberations and the discussions,
19 and I think it reflects it quite well. And I particularly
20 like the pesticide addition to the report.

21 CHAIRPERSON FROINES: Ellinor, in between taking
22 care of her newborn daughter, put in some very good work,
23 obviously on these and so we appreciate her efforts.

24 So, at this point --

25 PANEL MEMBER BLANC: Can I just -- this is a very

1 technical point but the only wording therefore that has
2 not gone on the record is actually the precise wording in
3 the arsenic box. And so I would just suggest the
4 following word change in the box, instead of
5 "...epidemiologic data on lung cancer," it would be
6 "...known human carcinogen based on epidemiologic data for
7 lung cancer..." and then the rest of the sentence would be
8 --

9 CHAIRPERSON FROINES: Well, I think that's okay
10 but I think that we then need to change the vinyl chloride
11 and benzene to be consistent with that.

12 PANEL MEMBER BLANC: Well, if you change the
13 vinyl chloride to insert the word "known" before the word
14 "human", then you would be consistent enough, I think,
15 throughout.

16 DR. FANNING: Okay. Then also the language in
17 finding 11 on PAHs to POM, you mentioned, John, that those
18 changes have been made, but it's not actually on the
19 record, so I don't know if we need to read through them
20 briefly. But just that where the findings in the
21 preceding version had been discussing polycyclic aromatic
22 hydrocarbons, that language has now changed to the correct
23 Toxic Air Contaminant Polycyclic Organic Matter. And I
24 believe that has been changed throughout.

25 There's still reference to PAHs in the finding in

1 situations where we're talking about specific research
2 studies looking at PAHs which are a subset of POM.

3 PANEL MEMBER BLANC: I think that's sufficient
4 without reading the actual changes, but I do think that
5 the -- I assume you were going to then have a formal vote.

6 CHAIRPERSON FROINES: We're about to.

7 Yes. Since we have comments on an individual
8 level from each member of the panel, we now need a motion
9 to adopt the findings.

10 PANEL MEMBER FUCALORO: So moved.

11 PANEL MEMBER FRIEDMAN: Second.

12 CHAIRPERSON FROINES: Any discussion?

13 All those in favor?

14 (Hands raised.)

15 CHAIRPERSON FROINES: The vote is unanimous.

16 Thank you very much.

17 This was a good effort, albeit difficult at
18 times.

19 Okay. So moving on Paul Gosselin and DPR are
20 going to update us on the organophosphate issues.

21 Is George here? Has George left?

22 I'm looking all around you. George, assume that
23 this letter on our SB 25 findings goes to Joan Denton, and
24 historically we would send our TACs to either Paul
25 Helliker or Alan Lloyd, is I assume this goes to Joan

1 Denton. I assume that we can also copy Alan Lloyd and
2 Paul Helliker as well.

3 DR. ALEXEEFF: I believe that's correct. It
4 actually goes to the Director of OEHHA. And the director
5 OEHHA has already sent a letter to Alan Lloyd as well, but
6 it would make sense for you to CC the Air Board as well.

7 CHAIRPERSON FROINES: And I'm assuming that we
8 will not CC Winston Hickox. We'll assume that Joan will
9 communicate our findings to Winston Hickox.

10 DR. ALEXEEF: Right. I don't know what your
11 normal process is for sending in comments.

12 CHAIRPERSON FROINES: We never have in the past.

13 DR. ALEXEEF: Right.

14 CHAIRPERSON FROINES: But SB 25 is a little
15 different than anything we've done previously, so that
16 we'll assume that you will send it forward.

17 Welcome.

18 Ready?

19 DR. PFEIFER: Sure. Good morning -- afternoon.
20 I'm Keith Pfeifer with the Department of Pesticide
21 Regulation. And I'm here today with Dr. David Rice from
22 OEHHA and we are the joint coordinators for this
23 cholinesterase work group project, and we will share the
24 presentation today.

25 (Thereupon an overhead presentation was

1 we call, an initial draft. And this is reviewed and
2 discussed by the cholinesterase work group, it's presented
3 by the lead author.

4 Then based on the discussion, suggestions,
5 comments, critique, we come up with what we call a revised
6 draft. And, at this point, we would consider informal
7 review, which can be done either by SRP members or also by
8 a few, what we call, external experts. And we did this
9 with two papers as far as the external experts.

10 On one paper on the functional observation
11 battery, we solicited comments from Ginger Moser, who's
12 one of the foremost experts in this area. On the paper on
13 analytical variability, we got comments back from Barry
14 Wilson at UC Davis and also Stephanie Padilla from U.S.
15 EPA who, I think, are two of the foremost experts there.

16 And they were quite willing to look at these
17 papers and give us good constructive comments.

18 CHAIRPERSON FROINES: What bullet are we are on
19 here? Are we on the third bullet?

20 DR. PFEIFER: Bullet number two.

21 CHAIRPERSON FROINES: Bullet number two, okay.

22 DR. PFEIFER: And then based on those comments,
23 we call the next draft a final draft based on the informal
24 review.

25 Now, our idea and our plan for the final draft is

1 the more specific areas that were to come.

2 So the first grouping has several papers on the
3 physiological, toxicological significance of
4 cholinesterase inhibition. And then as we move down the
5 list, some of the topics get more specific and more
6 important as far as developing eventual guidelines.

7 PANEL MEMBER FUCALORO: May I ask a question at
8 this point?

9 DR. PFEIFER: Sure.

10 PANEL MEMBER FUCALORO: Where in here will you
11 discuss the additive effects of people being exposed to
12 more than one toxin with the similar endpoint or --

13 DR. PFEIFER: The accumulative exposure, under
14 miscellaneous. And if you look at the --

15 PANEL MEMBER FUCALORO: Of course.

16 (Laughter.)

17 DR. PFEIFER: And I can just say briefly how that
18 evolved. If you look at the handout, the more detailed
19 handout, under that you'll see there's going to be a paper
20 authored by Dr. Ruby Reed in my group at DPR and Dr. Reed
21 is a member of the U.S. EPA Scientific Advisory Panel on
22 the cumulative guidelines that are currently being
23 developed.

24 And so she has firsthand information on where
25 they're going and the methodologies. And these guidelines

1 are due out in draft form, I believe, in December and we
2 will look at those and consider them in the context of
3 where we want to go. And Dr. Reed will subsequently
4 write-up a discussion paper on that.

5 And I know in March there was, I don't know
6 specifically, which panel members here brought this up.
7 It may have been yourself, Dr. Fucaloro, but I know Dr.
8 Byus, in subsequent discussions, wanted that topic added
9 to our group. So that's one reason that we're including
10 it.

11 PANEL MEMBER FUCALORO: Thank you.

12 CHAIRPERSON FROINES: As long as we're on this,
13 what would you prefer, would you prefer that you go
14 through the entire presentation and then take questions or
15 take them as we go along?

16 DR. PFEIFER: Yeah, I think the former, because
17 I'm going to turn it over to Dr. Rice now and let him go
18 through and --

19 CHAIRPERSON FROINES: Go through the whole thing
20 and then questions.

21 DR. PFEIFER: And then if you have some that
22 would be great.

23 DR. RICE: Hi. I'm Dave Rice from OEHHA. Is
24 that loud enough?

25 I'm just going to take a couple of minutes here

1 and present some information regarding the progress we've
2 made, what we need to do and what we're doing right now.
3 And if I could have the next overhead.

4 --o0o--

5 DR. RICE: It's pretty straightforward, referring
6 to the list of all the individual discussion papers that
7 you've been provided with in the handout. Of the 27
8 papers, or 27 different discussion papers listed in that
9 handout, we've completed final drafts on 19 of them, and
10 they're ready for either SRP and/or external review. We
11 have five drafts that are at various stages that have
12 already been presented to the work group. And no
13 revisions are in progress.

14 And we have three drafts that have yet to be
15 presented to the work group, but they're scheduled to be
16 completed by the first week or first meeting or so in
17 January, I believe.

18 --o0o--

19 DR. RICE: On the next overhead it gives you an
20 idea of what we still need to do, and obviously we need
21 to, the first bullet, finish our discussion papers. We
22 need to complete the review of those discussion papers by
23 the Scientific Review Panel and/or external experts. The
24 next bullet we need to, or actually we have already
25 established risk assessment guideline categories for

1 grouping of the questions that have been developed as a
2 result of the individual papers. And I'll talk about that
3 more on the next overhead, but I don't want to go to it
4 yet.

5 I will say that, you know, what we've come up
6 with as a process is it's pretty clear that our guidelines
7 are going to be a result of the discussions that come out
8 of these issue questions that are at the end of each
9 paper.

10 So we wanted to kind of formalize our approach to
11 talking about those particular issues, and so we've
12 established -- we revisited the topics that we have for
13 the individual papers, taking a look at the questions that
14 have come out of the individual papers and reprioritized
15 the various topics based on that information and our needs
16 in terms of risk assessment.

17 And, again, I'll talk about that a little bit
18 more on the next overhead.

19 The next bullet we're going to go through those
20 guideline categories after we've plugged in all the issue
21 questions and consolidate those questions and eliminate
22 duplications and set aside any questions that may not be
23 particularly relevant to our needs.

24 We then also need to formulate the
25 recommendations based on discussion of those issue

1 questions. We still need to determine really the scope
2 and the format of our actual product is are we going to
3 end up with two documents. One document that's going to
4 be all the discussion papers and another document that's
5 going to be guidelines, you know, being connected with
6 some sort of executive summary or have one big document.
7 We're just not quite sure what the final product is going
8 to look like.

9 And then, of course, after we get past that, we
10 are going to need to present our guideline recommendations
11 to this panel.

12 --o0o--

13 DR. RICE: The next overhead, which is pretty
14 busy, but I'll try to get through it real quick, is this
15 is just our grouping for the issue questions that have
16 come out of the discussion papers. And we have four main
17 headings, as you can see. We've got the relevance of
18 cholinesterase inhibition to risk assessment. We
19 obviously thought that was a most important question to
20 ask here. Something that has come up out of our
21 discussions is the next major heading and that's the use
22 of human cholinesterase data, since more and more human
23 data is being submitted in the area of pesticides in
24 support of registration.

25 Our next major topic area is, you know, how are

1 we going to deal with the LOAEL/NOAEL determination, and
2 the impact of analytical variability, biological
3 variability, biological significance and what kind of
4 uncertainty factors we need to apply.

5 And the last major grouping is the relationship
6 of cholinesterase inhibition to other endpoints, such as
7 endpoints we see in the functional observational battery,
8 developmental neuro-toxicity, ocular toxicity,
9 immuno-toxicity, endocrine disruption and structure
10 activity relationships, that's really not an endpoint, but
11 we included that there just so we can continue or finish
12 our discussion on the topic.

13 And that's pretty much all I have. I guess if
14 there are any questions.

15 CHAIRPERSON FROINES: Thank you. Could we have
16 the lights.

17 PANEL MEMBER BLANC: So the relationship between
18 the working papers and then this final slide is that
19 multiple group papers would inform the same or overlapping
20 topics.

21 DR. RICE: Exactly, and vice versa, I guess
22 that's the overlapping part. A given set of issue
23 questions from the paper may plug into different topics as
24 well.

25 PANEL MEMBER BLANC: Well, just looking at the

1 outline of the discussion papers, one of the things that
2 may come up as a possible source of unnecessary confusion
3 may be times when you're using cholinesterase as an
4 umbrella term in times when you're using
5 acetylcholinesterase specifically and
6 butrylcholinesterase, so you might want to just go back
7 and make sure that you're consistent in your terminology.

8 DR. RICE: Certainly.

9 DR. PFEIFER: Yeah, I think when we use the term
10 cholinesterases, it means all of them, and then we try and
11 be specific. And I know in developing our risk
12 assessments that question has come up. And generally my
13 suggestion in some cases is to clearly define which
14 cholinesterases you're talking about, just so there isn't
15 any misinterpretation.

16 PANEL MEMBER BLANC: Right. Because, for
17 example, topic 2C.2 Acetylcholinesterase in Neural
18 Development. I assume you would be concerned about neuro
19 target esterase and neuro development also, so that
20 implies you're only looking at cholinesterase and others,
21 and then you talk about acetylcholinesterase in topic
22 2C.4, when I guess you mean cholinesterases. I mean, you
23 should try to be consistent, because you're going to
24 engender unnecessary confusion, I think. At least when it
25 comes back to us, it may be confusing.

1 Now, also about that is just in how you've
2 divided things up. For example, Topic 1C, which is
3 Acetylcholinesterase in Different Brain Regions, and then
4 the next one is Cholinesterase Inhibition in Blood and
5 Peripheral Tissues. Is the implication that the
6 peripheral nervous systems is going to be covered in 1D or
7 that the peripheral nervous system is not a different
8 brain region. So it's odd in that constellation that
9 there is not a separate peripheral nervous system paper
10 then or -- do you see what I'm asking?

11 DR. RICE: Yeah.

12 DR. PFEIFER: Not entirely on the latter. I'm
13 trying to focus in on the consistency with the
14 terminology.

15 PANEL MEMBER BLANC: Well, you're dividing up the
16 physiologic significance of cholinesterase inhibition in a
17 broad way. And so you've got one paper that's going to be
18 on the central nervous system, I guess, because when you
19 say the brain, I assume you mean the central nervous
20 system.

21 DR. PFEIFER: Specifically the brain. And in the
22 blood, I believe, the focus was on acetylcholinesterase,
23 but sometimes its blood measures both butryl --

24 PANEL MEMBER BLANC: And so where would the
25 peripheral nervous system be?

1 DR. PFEIFER: Pardon me?

2 PANEL MEMBER BLANC: Where would the
3 peripheral --

4 DR. PFEIFER: Oh, the peripheral tissue such as
5 the lung and diaphragm, that's one area.

6 PANEL MEMBER BLANC: So you're saying that topic
7 1D would address the peripheral nervous system?

8 DR. PFEIFER: Well, peripheral tissues,
9 specifically lung, diaphragm, because one of the areas of
10 interest is developing formats methodological for and
11 requiring that for submission for registering a pesticide,
12 and as an indication of peripheral cholinesterase
13 inhibition.

14 PANEL MEMBER BLANC: Well, I guess what I'm
15 trying to say as you're going to be presenting it to us,
16 there are going to be issues that are going to be
17 classically related to sites of neuro transmission, and
18 then there are going to be cholinesterase effects in ways
19 that are not related to neuro transmission, I suppose.

20 DR. PFEIFER: Well, that one is related to neuro
21 transmission.

22 PANEL MEMBER BLANC: However you slice up the
23 pie, there will need to be some clarity for the people
24 receiving these, so that they understand what's included
25 and what isn't and to make sure that everything is

1 covered.

2 CHAIRPERSON FROINES: But I think that there's an
3 approach that relates to the science and there's an
4 approach that relates to regulatory demands. I think the
5 generic term is the peripheral nervous system, and I think
6 within that generic concept then there may be specific
7 tissues that have more specific relevance. And it seems
8 to me that it's in that order that one wants to address
9 it. I think that's what Paul is saying.

10 PANEL MEMBER BLANC: Well, what I can't tell you
11 that topic 1D is what it actually covers. All I'm saying
12 is that here I'm looking at this title of what this
13 working paper is on, and I have no idea what you mean,
14 because I'm coming at it from a different disciplinary
15 point of view.

16 DR. PFEIFER: Well, quite frankly, when I made
17 this list up, I went back and looked at some of the
18 titles. And I had to kind of clarify them a little bit
19 too, because they weren't that specific from my
20 interpretation, so I understand that.

21 CHAIRPERSON FROINES: But I think the 1C, when
22 you say, again, the generic term is the central nervous
23 system, the specific term is various brain regions. I
24 think one wants to make sure that the broad title is the
25 starting point and the details come below.

1 DR. RICE: I would agree. I think we need to go
2 back and look at those, because we do discuss the CNS and
3 the peripheral system in both of these papers or in either
4 one of the appropriate papers. And we need to make sure
5 that we address it completely and, you know, be precise
6 about our title.

7 PANEL MEMBER BLANC: Because the problem is how
8 will you know that you haven't missed a topic, because one
9 person thinks they're doing it and the other group thinks
10 that the other group is doing it based on --

11 DR. PFEIFER: There will be some overlap, but we
12 tried to get pretty focused on, you know, this specific
13 one.

14 PANEL MEMBER BLANC: You know, I'm actually less
15 worried about overlap than I am about something getting
16 not addressed.

17 DR. PFEIFER: We haven't missed very much, if
18 anything, believe me.

19 CHAIRPERSON FROINES: But I think that this body
20 is a body of scientists not regulators. And so to the
21 degree that there are specific issues about registration,
22 approval, regulatory considerations, then that needs to be
23 a subset where you're educating the panel about those
24 specifics, because you can't assume that scientists in
25 universities or this panel or in general will necessarily

1 be knowledgeable about those more --

2 DR. PFEIFER: I hope I didn't, you know, mislead
3 you on that, when I was talking about this peripheral.
4 No, these papers don't get into, you know, any regulatory
5 or registration type.

6 PANEL MEMBER BLANC: And then topic 4A
7 Organophosphate Toxicity Heterogeneity in Humans.
8 Conceptually, what is that addressing?

9 DR. PFEIFER: Variability in the human
10 population.

11 PANEL MEMBER BLANC: I mean, is it narrowly a
12 genetic variability or are you addressing age variability
13 in responsiveness or --

14 DR. PFEIFER: I think both.

15 DR. RICE: As I recall the paper, we addressed
16 just variability in humans as a broad stroke. And any
17 sort of information we could collect on variability,
18 particularly in terms of response, that that's what's
19 included.

20 PANEL MEMBER BLANC: So it includes both
21 sensitivity and susceptibility?

22 DR. RICE: Correct.

23 DR. PFEIFER: And then if you look at Group 8,
24 these two papers are in the category of still being
25 developed and there will be some information there that

1 will relate back to topic 4 and 4A.

2 PANEL MEMBER BLANC: Because you already had a
3 question, I guess, about topic 9A, but if you think about
4 looking ahead to see what are the errors in which we have
5 to grapple at this end or are likely to be raising
6 questions on individual chemicals as they come forward,
7 these are the more difficult areas that we face and are
8 likely to be areas of particularly intense concern.

9 DR. PFEIFER: You mean the human susceptibility
10 and sensitivity?

11 PANEL MEMBER BLANC: Yes. They're generic. I
12 mean they're not specific -- they're not as specific to
13 this as obviously the issues about what does it mean to
14 measure butrylcholinesterase versus acetylcholinesterase
15 or any of these other questions. But nonetheless, they're
16 quite relevant.

17 I would encourage you to throw a broad net in
18 that particular evaluation, and look very closely at not
19 just age and genetic factors, but also look at nutritional
20 status and some of the other things that have been areas
21 of concern, particularly in cholinesterase inhibition
22 effects.

23 Time line to the panel. I mean, when would we be
24 likely to need to be thinking about a workshop or
25 discussion time or agenda time?

1 DR. PFEIFER: Well, we talked about this briefly
2 this week, and based on the task in front of us, not so
3 much the discussion papers, but discussions on developing
4 recommendations of the guidelines and then having some
5 type of external review, we're probably looking at the
6 second quarter of 2002, probably at the end of the second
7 quarter, so it would be close to June, I would think.

8 PANEL MEMBER BYUS: Your original time line was
9 now, right. I'm not saying anything.

10 DR. PFEIFER: Actually, I looked at that.

11 PANEL MEMBER BYUS: It was a little optimistic.

12 DR. PFEIFER: No, I looked at that. And the
13 fourth quarter of 2001 I said finish discussion papers,
14 which, you know, we're probably a month behind there. And
15 it said start formulating guidelines. And we've already
16 started doing that, but I think there's, you know, going
17 to be quite a bit of discussion and work ahead.

18 There are some papers that are quite important to
19 this whole thing that are being revised, so that we can
20 call them a final draft. And I think it's appropriate to,
21 you know, where needed, that they be revised, because in
22 our workgroup there is a lot of open discussion a lot of
23 individual opinions presented about, you know, people's
24 perceptions, concerns and scientific opinions that all, I
25 think, added to the quality of these papers.

1 So, yeah, you're right, we probably were a little
2 optimistic. But the idea of having, what I would call,
3 experts outside the regulatory community pretty much
4 review these, I think, would add a tremendous amount of
5 credibility to not only the papers, but to the eventual
6 recommendations, because obviously the people are going to
7 take this information and compare what we have come up
8 with directly with what the federal government has come up
9 with and how to apply it.

10 And that has been, you know, my goal from the
11 beginning to have it as best a footing on science to
12 develop these as possible. And I think, like I said, we
13 had Stephanie Padilla and Barry Wilson and Ginger Moser
14 look at our papers, and I can tell you that their comments
15 were quite favorable, but they were also very pointed in
16 their critique of some of the things that they didn't
17 agree with.

18 CHAIRPERSON FROINES: I have a number of comments
19 that I'd like to -- some are substantive, some are
20 procedural.

21 The first thing I think I'd like to ask you to do
22 is, I think, there needs to be a Chapter 1. And Chapter 1
23 needs to lay out the issues that will be dealt with in the
24 subsequent list of papers and the overall objectives of
25 the exercise in producing these documents. And I'm not

1 talking about an executive summary.

2 I'm talking about Chapter 1 should tell the
3 reader, tell the public what are the issues that are going
4 to follow in these, however many, documents there are and
5 that will be addressed and what are the fundamental issues
6 that we are -- why this is going forward?

7 In other words, to tell the reader in Chapter 1,
8 in essence, the basis, the objectives for everything that
9 is to follow. There needs to be obviously an executive
10 summary produced separately than that. But, I think, at
11 the outset, we need to inform everybody about why are
12 there now 12 to 15 to 19 documents that are going to
13 follow, and what are the very specific issues. And so
14 that's the first point.

15 I think the last chapter obviously has to be, and
16 I assume that that's what you were going to do, is I'm
17 not -- I don't think I agree that the last chapter is
18 cholinesterase issues, questions for guideline
19 development. I think the last chapter has to be your
20 recommendations for the guidelines.

21 DR. PFEIFER: That wasn't meant to be the last
22 chapter. That's just in each individual paper, that's the
23 last part that gets extracted out for using the
24 guidelines -- developing the guidelines.

25 CHAIRPERSON FROINES: So the first chapter tells

1 everybody what it's all about. The last chapter tells
2 everybody where you've come to. And in between you
3 develop the scientific basis for that, so that they're
4 basically -- this is basically a three-part per exercise
5 as I would look at it. And I think that will help clarify
6 it, because the current first chapter which I've read
7 starts out going through the physiologic consideration of
8 acetylcholinesterase, and then at the end of the document,
9 it gets into various policy issues.

10 And so you kind of have a little bit of apples
11 and oranges in the first chapter, and I think it's
12 important to be able to make sure that people understand
13 what the procedural policy, scientific questions are that
14 need to be addressed and then get into the actual
15 technical details.

16 The second thing that I wanted to say is I think
17 that, as far as I'm concerned, obviously this is your
18 process and you can invite external experts all you want
19 to help you as you go forward, and I certainly would
20 support that and encourage it.

21 I think in the end, I would like to propose a
22 joint effort. And that is in the end, at the end,
23 however, you may have gotten Stephanie Padilla to look at
24 five chapters in the beginning or Barry or whoever, but in
25 the end before the document -- the final draft review, I

1 think that should be, in essence, a joint effort between
2 the SRP, OEHHA and DPR.

3 And that what we do is the SRP -- because this is
4 going to help us do the review, and that's what I'm
5 thinking about. I'm trying to think about how are we
6 going to review 20 documents with this small panel. So
7 what I would propose is that at the final draft review
8 stage that we put together a list that comes from this
9 panel, from DPR and from OEHHA.

10 And out of that list, we develop a final list of
11 external experts who we want to review the document. We
12 send it out and we get their comments back and then you go
13 back and make changes, and then the final document comes
14 forward.

15 So something like that so we are all participants
16 in defining who the external experts are, because I think
17 that will benefit this panel. And so we'll have
18 confidence that we've come up with a list of names and
19 OEHHA has come up with a list of names and so on and so
20 forth.

21 DR. PFEIFER: I think that's fine. I mean,
22 that's something I probably wasn't very clear on, but
23 certainly, you know, I think that would be a good idea.

24 CHAIRPERSON FROINES: The third thing that I'd
25 like to say, and this is not a criticism meant at all, it

1 is an attempt, on my part, to preserve the energy level of
2 the SRP participants, and to, in a sense -- but more
3 importantly that the role of the panel is to review a
4 document in terms of its adequacy. And I don't know the
5 exact statutory language, but I think we have to be
6 careful to preserve our review function from our being
7 intimately involved in the document development.

8 In other words, I want to keep Craig Byus from
9 performing a staff function for DPR and OEHHA, because
10 that then makes it harder for him to be an independent
11 reviewer when the document actually comes to us.

12 He may not agree, but I think that we just have
13 to be careful. We also have to make sure we don't wear
14 him out, by the time -- so when he comes here with the
15 final document, he's able to be an objective thinker about
16 it.

17 So I would suggest that during the document, when
18 you're going through multiple drafts, and this is -- I
19 mean, I'm just suggesting this. The panel has to decide
20 how it wants to deal with the lead person. That's up to
21 the panel. But I would suggest that the panel not be as
22 deeply involved in the various chapters as one might
23 think, because there may be multiple drafts and what have
24 you, but that the panel more or less reserves itself to
25 the final draft review, so that when we're having these

1 outside speakers do the review, we also have the leads
2 doing the review at that point.

3 So that, in a sense, the SRP reviewers are in
4 sync with the external reviewers, and that's a kind of
5 dynamic process. And that's different than say Craig
6 being involved in draft 3 of Section 2B.2.

7 And so I would say that the SRP leads would play
8 their most important role at the final draft review when
9 also the documents were going out to external reviewers
10 would be my suggestion.

11 And so I think -- pardon me, I made some notes.

12 I think that covers it from my standpoint. I
13 think the only other thing that is a matter of concern to
14 me, and this is opening Pandora's Box, and I admit that
15 I'm doing it, is when we have -- when the panel had the OP
16 workshop last year, one of the key questions that we asked
17 that really wasn't dealt with very effectively, and it
18 came at the end of the day, was toxic effects associated
19 with cholinesterase inhibitors, but that are independent
20 of cholinesterase inhibition.

21 In other words, we have a whole spectrum of
22 effects associated with cholinesterase inhibition, but are
23 these compounds capable of causing toxicity via other
24 mechanisms, even in addition to delayed neuro-toxicity?

25 And you haven't really got that in here. It

1 seems to me -- or at least, I missed it. But it seems to
2 me that the sort of other toxic endpoints via other
3 mechanisms is an issue of -- that we shouldn't not address
4 those. Those are my comments.

5 DR. RICE: Well, with respect to the last
6 comment, we agree completely and we do -- we are
7 attempting to look at any other forums of toxicity for
8 these particular compounds as we're reviewing the
9 literature.

10 And in the -- I don't know what the best -- in
11 the risk assessment guideline categories for the issue
12 questions, the very last category, to a large degree
13 addresses that, where we look at the relationship of ChE
14 inhibition to other endpoints, and that means in terms of
15 sensitivity.

16 CHAIRPERSON FROINES: Where am I looking?

17 DR. RICE: Oh, the very last overhead where we
18 look at things such as ocular toxicity, immuno-toxicity,
19 endocrine disruption, and, you know, the reasons down at
20 the bottom of the list, so far we haven't seen any
21 indication of any of these aspects of toxicity from these
22 compounds to be anymore -- or to be more sensitive than
23 inhibition of the different cholinesterases.

24 So, in a general sense, we're looking at that.

25 CHAIRPERSON FROINES: Yeah, be careful, because

1 you're making a judgment about -- you're doing risk
2 assessment at the same time that you're doing -- by the
3 sentence, by saying if you're considering sensitivity,
4 you're making a judgment call there, I think.

5 DR. RICE: Right.

6 CHAIRPERSON FROINES: But I read this -- but this
7 relationship of cholinesterase inhibition to other
8 endpoints, I'm saying it differently. I'm saying
9 relationship of cholinesterase inhibitors to other
10 mechanistic pathways leading to other endpoints.

11 DR. RICE: Oh, I understand. And that's why I
12 couched that, in terms of -- the risk assessment in terms
13 of sensitivity.

14 DR. PFEIFER: I mean, obviously, the focus of
15 this work group was on the inhibition of cholinesterase.
16 So the question was are there other -- you can
17 characterize types of systemic toxicity that are or are
18 not related to cholinesterase inhibition. So that was
19 basically the question before the authors. And so they
20 went through the literature and looked at those aspects.

21 PANEL MEMBER BLANC: Well, perhaps the way of
22 melding these two things together would be in the
23 introductory section that Dr. Froines has alluded to, if
24 you're in agreement with drafting such a section, that it
25 would delineate both the terminology and the potential

1 mechanistic implications.

2 Because there are really three things that are
3 embedded in what we're talking about. One would be
4 toxicity related to cholinesterase inhibition at sites
5 other than sites of neuro transmission, that would be
6 inhibition of cholinesterase with effects that the
7 cholinesterases have that are unrelated to neuro
8 transmission.

9 The second would be inhibition of other enzymatic
10 functions that are not precisely cholinesterases.

11 And the third would be toxic effects completely
12 independent of enzymatic inhibition that it has a
13 structural, functional relationship to cholinesterase like
14 structures, I guess.

15 Those are three possible different path ways.
16 And as you get farther away from anything resembling
17 cholinesterase inhibition then there's less and less data,
18 and less and less likely to be broad links, that there may
19 be one acetylcholinesterase inhibitor which on an
20 idiosyncratic basis, tends to be a sensitizer because of a
21 side group, and can't really generalize to other
22 acetylcholinesterase inhibitors, because it's a
23 peculiarity of that particular one for all I know.

24 So I suppose as you get farther afield, it's less
25 generalizable, where I wouldn't see any reason why this

1 shouldn't be a general pattern of effects.

2 Does what I'm saying fit into your -- does that
3 correspond to your, sort of, categorization or one way of
4 categorizing it or is there a space in one of these
5 documents where those issues are delineated?

6 DR. PFEIFER: I don't know that we're considering
7 looking at how you characterize other enzymatic -- I mean,
8 we're considering looking at the inhibition of
9 cholinesterase certainly as an endpoint. And then we
10 wanted to look at other types of, what I would call,
11 systemic toxicity and see if we could say that was related
12 to cholinesterase inhibition or it was independent of
13 cholinesterase inhibition.

14 And then the next question would be, are these
15 other endpoints of toxicity as sensitive, more sensitive
16 or less sensitive than the inhibition of cholinesterase
17 for risk assessment purposes?

18 CHAIRPERSON FROINES: I understand that. I think
19 coming from a toxicologic standpoint, one of the questions
20 I'd be interested in then though is what are the
21 mechanistic considerations that suggest, that underlie
22 other systemic toxicity that might occur separate from
23 cholinesterase inhibition.

24 DR. PFEIFER: And where known, that is addressed.
25 If it isn't known, then --

1 DR. RICE: We do address those three areas that
2 you talked about. We don't specifically identify them as
3 such. But as an example, in one of the papers on
4 butrylcholinesterase, there's a discussion of the
5 potential stereo chemical role, if you will, that
6 butrylcholinesterase may have in neurodevelopment, for
7 instance, and/or in nervous system transmission, not an
8 enzymatic role or actually an unknown role.

9 In the paper on immuno-toxicology,
10 immuno-toxicity of the Cholinesterase inhibitors, there's
11 a very large discussion of the effect of cholinesterase
12 inhibitors inhibiting enzymes important in the immuno
13 response that aren't cholinesterase, but other --

14 PANEL MEMBER FUCALORO: That are not.

15 PANEL MEMBER BLANC: Yeah, there are other
16 esterases.

17 DR. RICE: Other esterases of unknown, you know,
18 function and known function. And so we address those
19 issues as we find out information in each of the topic
20 areas.

21 DR. PFEIFER: But they are specific to the topic,
22 which is, I think, what you were getting at, and not just
23 other general toxicity.

24 DR. ALEXEEFF: George Alexeeff with OEHHA, just a
25 point of clarification, now there's two ways one could

1 approach this overall issue. One is to develop guidelines
2 for cholinesterase inhibitors. In other words, chemicals
3 that cause inhibition, but that may or may not have the
4 sensitive most sensitive health effect or the most
5 important health effect, which is, I think, what you're
6 referring to.

7 The other is to come up with guidelines on if
8 you're evaluating cholinesterase inhibition, how you
9 actually do that. You know, what would the procedures for
10 evaluating that?

11 And I think what staff has indicated that they're
12 looking at other endpoints, but at the same time that
13 they're looking at these particular compounds to see how
14 cholinesterase plays out in terms of other endpoints.

15 But I guess my question comes back with the panel
16 in terms of just your expectations as to what you think
17 this work product will look like, is it your expectation
18 that, okay, if we're taking a particular cholinesterase
19 inhibitor, what will be the guidelines in evaluating it?
20 In other words, how will we look at cholinesterase and how
21 will we make sure that there isn't some other endpoint
22 missed?

23 That's why it's not clear, when you're bringing
24 up these other endpoints, that by working out other
25 mechanisms, which are important, we might normally do that

1 in our normal evaluation of any TAC. You know, we'd
2 always like at -- for example, we looked at death and
3 carcinogenicity was the endpoint.

4 So that's why, I guess, it was not clear and not
5 to try to expand the scope of this series of work
6 products.

7 CHAIRPERSON FROINES: Well, I think that's a good
8 point. And that's why even when I raised it, I raised it
9 with some hesitation. But I think that clearly there has
10 been some debate and controversy, or however one wants to
11 phrase it, about cholinesterase inhibition in and of
12 itself. So that's a box that we can clearly recognize
13 that we want to address from a risk assessment standpoint,
14 risk assessment methodology standpoint.

15 But we also don't want to just look for the keys
16 under the light-post either, because people have been
17 looking at OP compounds in terms of cholinesterase
18 inhibition for the last umpteen million years. And so we
19 keep looking at that and should. But the question is, are
20 there other keys out there in the darkness that we're
21 missing, and that's what I think we can't simply avoid,
22 because I think that could lead to an error in --

23 DR. ALEXEEF: I think that would normally be
24 picked up on a case-by-case evaluation of the compound
25 hopefully. Granted, there may be some overreaching

1 issues, but that would be pretty hard for us to look at
2 all cholinesterase inhibitors and come up with a list of
3 likely other noncholinesterase things that could also
4 happen in the document, I mean, like this.

5 But I think that maybe we could somehow in, as we
6 formulate the guidance, be clear that just because
7 something inhibits cholinesterase, that's not necessarily
8 what the ultimate NOAEL development will be based on,
9 because that may not be the most important relevant,
10 sensitive or appropriate endpoint.

11 DR. PFEIFER: Well, also not all the
12 cholinesterase inhibiting compounds exhibit a lot of these
13 other systemic toxicities, liked delayed neuro-toxicity,
14 ocular toxicity and some of these other points.

15 PANEL MEMBER BLANC: Well, I mean let's come back
16 to that as a good example. Let's talk about delayed
17 neuro-toxicity in response to your question, George. I
18 think that this panel, whenever organophosphate comes
19 forward, is going to want to know if the appropriate tests
20 were done that had evaluated its potential for delayed
21 neuro-toxicity.

22 And to the extent that these documents illuminate
23 what is the best way in which one assesses neuro target
24 esterase effects, that is something that we'll be for.

25 The parallel to that would be if there is a

1 generalizable structure function effect that
2 cholinesterase inhibitors have on an esterase, which is
3 present in leukocytes and which can be related to antigen
4 presentation. Then we need to know about that so that
5 every time a cholinesterase inhibitor chemical comes
6 forward, we say have the appropriate tests and structure
7 function assays been looked at.

8 What I think there's less need for and less
9 interest in the panel would be a sort of idiosyncratic
10 miscellaneous effect of a peculiar cholinesterase, which
11 has a very odd side group, which is associated with met
12 hemoglobin emia, but in no way do the data suggest that
13 the class, even a subgroup of acetylcholinesterase
14 compounds, cause met hemoglobinemia. Is that helpful to
15 you?

16 DR. ALEXEEFF: Yeah, and I think we've tried to
17 address that. You can see how some of the topics are set
18 up. I'm just looking at like 2C.3, Ocular Toxicity
19 Associated with Organophosphate Exposure.

20 That's not necessarily only cholinesterase
21 mechanism. Maybe it is, I don't know. I don't know the
22 literature. But I'm just saying we could look at ocular
23 toxicity, in general, since that is an effect that occurs
24 and look for things that you're, you know, mentioning that
25 may be there's some other generalized effect that occurs

1 possibly --

2 PANEL MEMBER BLANC: But look at 2C.4,
3 acetylcholinesterases and the Immune System. The title of
4 that suggests that the only esterases for which the
5 discussion there would focus on would be
6 acetylcholinesterase and the immune system.

7 I understand from your oral comments that, in
8 fact, you'd be looking at other enzymatic effects of
9 chemicals which are acetylcholinesterase inhibitors. And
10 comes back to my earlier comment about being sure that the
11 titles of your topics or the subtitles, you should make it
12 clear how you're dividing up the pie, so that we're
13 assured that everything that we want to be covered is
14 being covered.

15 DR. RICE: We do need to be more precise, because
16 a more appropriate title for that particular paper would
17 be something like effects of cholinesterase inhibitors on
18 the immune system. And that would take into account any
19 effects it may have on other enzymatic processes.

20 CHAIRPERSON FROINES: I did not understand what
21 you just said.

22 DR. RICE: What I said was changing the title.
23 Instead of saying acetylcholinesterase is in the immune
24 system, the effect of cholinesterase inhibitors on the
25 immune system would not limit it just to

1 acetylcholinesterase, nor would it limit to --

2 CHAIRPERSON FROINES: But the question is the
3 cholinesterase inhibitor operating via noncholinesterase
4 inhibition mechanism may produce immuno-toxicity.

5 DR. RICE: I understand that.

6 PANEL MEMBER BLANC: It's not easy. To get the
7 right wording it's not -- it's completely convoluted and
8 laborious, but you can see the problem here.

9 CHAIRPERSON FROINES: So, for example, for 20
10 years, I think it's getting 30 years now I've been
11 interested in issues of degeneration, and I've always been
12 a skeptic about neuro target esterase, because I think
13 it's too simple a view of that process.

14 And so I, in my own personal professional
15 scientific career, have been interested in OP compounds
16 that have some potential or exonil degeneration. And so I
17 continue to have that kind of interest, and I'm not
18 pushing it on you, but it's just an area that I think we
19 don't want to exclude, even though we recognize that we
20 have these key questions around cholinesterase inhibition
21 to answer.

22 Can I ask -- I want to ask Craig Byus a question,
23 because I propose, basically, that the panel leads play
24 their most dramatic role at the final draft review stage.
25 And, actually, Craig can do as much as he wants in

1 between. That's clearly up to him as an individual
2 investigator. But are you comfortable?

3 PANEL MEMBER BYUS: I was going to ask you for
4 that guidance today, in actuality, and what level, how
5 each detail Peter and I should spend during this process?

6 Let me say I think the process is going along
7 well. I mean, I have all of the chapters. I was much
8 more proactive in the beginning in reviewing these
9 chapters than I have been lately, simply because of the
10 amount of effort and time that it takes.

11 And I think it's going along well. I think
12 there's a problem -- I see there are several problems.
13 One is this sort of bottom up approach as opposed to a top
14 down approach. We would like to see sort of a global
15 overview and defining of the key issues, and then a
16 working down from the top.

17 And their approach, this is my own opinion, it's
18 been more from the bottom up, these guys are in the
19 trenches working with this day to day all the time, year
20 after year. And so they have a lot of procedural issues,
21 which have a lot of scientific basis, and so they're
22 looking at it pretty much, sort of, from the bottom up.

23 I think that's fine. I originally thought top
24 down was better, but as I read these things, I agree
25 there's sort of a dichotomy between what's in the titles

1 of these chapters and what's actually here, so that
2 there's a lot of editorial work that's going to have to be
3 done ultimately.

4 But I think the process is ultimately fine. I
5 think that going from the bottom up will ultimately work
6 out, bottom up will work out fine, if somebody at the end
7 does what you suggest with Chapter 1, does a big global
8 overview and really does do the editorial job that's going
9 to need to be done to tie everything together.

10 And consistency, this was another problem I had.
11 It's great to have all these people doing this, and I
12 really applaud this, because I think it does bring in all
13 of these other viewpoints.

14 But it makes it more difficult from an editorial
15 consistency point of view to make the kind of document
16 that we would all like to see here, as a university
17 professor and whatever, so that's going to be one of your
18 problems, I think, ultimately. So how you solve that, you
19 know, it's going to be somewhat difficult, but that's what
20 I foresee.

21 And then the other big thing is the policy
22 issues. I mean, I really think the policy issues, when
23 you have the science here, and it may be spread apart in
24 various places, but really the science is good, the
25 references are good. It's kind of the classic old

1 pharmacology coupled with toxicology, and a lot of these
2 as you know -- as you said a lot of these issues have not
3 been resolved. Relatively simple things you would think
4 could have been resolved many years ago have not been.

5 And I think really the key thing is going to
6 be -- one of the key things is going to be the policy,
7 what you have developed as policies, and that's where we
8 need to really -- I don't know whether -- so I would say
9 to you, I agree about allowing them to develop this
10 document as they want and -- but are they going to want
11 our input before they develop the policy, that's where I
12 see maybe we could put some input in --

13 DR. PFEIFER: Well, our goal --

14 PANEL MEMBER BYUS: -- before or after. But I
15 mean that is the key thing, because you're going to come
16 back and you're going to say butrylcholinesterase is
17 irrelevant, and it means nothing. Now, that's what you've
18 said in the past. Now, clearly, I would disagree with you
19 with this.

20 So if that's your policy, that's where we're
21 going to be -- and maybe that is the best time to argue it
22 out, after you have developed the policy and after there
23 is the document with the data here in front us that we can
24 all look at.

25 DR. PFEIFER: I think our goal is to give you

1 recommendations, which will be guidelines/policy

2 recommendations, and then --

3 CHAIRPERSON FROINES: I would like to actually
4 disagree with something Craig just said. I would almost
5 like to avoid the word "policy", because that sounds like
6 something that we should give a call to Paul Helliher and
7 ask him what he wants to do or Winston Hickox, and I don't
8 want to do that.

9 DR. PFEIFER: This is a guideline.

10 CHAIRPERSON FROINES: Exactly why I want to stay
11 away from the concept of policy, because what I would like
12 and I think this panel has an obligation to view it this
13 way, is that based on the science comes recommendations
14 for how to approach risk assessment, and then we can
15 debate that.

16 We may have the head of Cal EPA may decide as a
17 matter of policy to change all that. That's a different
18 issue. I think ours should be based on the review of the
19 science rather than a review of somebody's point of view
20 on this subject.

21 So I think what we need to do is to have the
22 forest, then we have the trees, and then we have the
23 forest again with what --

24 (Laughter.)

25 PANEL MEMBER FUCALORO: This is Chapter one

1 little chapter zero.

2 (Laughter.)

3 PANEL MEMBER BLANC: You're the Lumber Jack?

4 (Laughter.)

5 PANEL MEMBER WITSCHI: Well, except it's going to
6 be the second forest after the beavers have gone through
7 it.

8 (Laughter.)

9 PANEL MEMBER FUCALORO: That's appropriate, we're
10 talking about pesticide.

11 CHAIRPERSON FROINES: Well, we can get lost in
12 any one of those three places. As we've seen, we can get
13 lost pretty easily.

14 I had a question about where -- since I think
15 that toxicokinetics are really quite crucial to
16 cholinesterase inhibitors. Is toxicokinetics incorporated
17 within these sections or is there going to be separate
18 discussion of toxicokinetic issues?

19 DR. PFEIFER: Well, you have to understand in
20 looking at these papers as well as all the other things I
21 believe that Drs. Kellner and Moore in Topic 1A went
22 through some of the toxicokinetics.

23 DR. RICE: Dr. Byus disagrees.

24 PANEL MEMBER BYUS: I'm trying to remember.

25 CHAIRPERSON FROINES: I read 1A, if that's -- I

1 wouldn't agree with that.

2 DR. PFEIFER: I know there is some papers where
3 there's a lot of enzymatic, but I can't recall specifics.

4 DR. RICE: I can't recall specifically either,
5 but I think it more -- it would tend to be towards the
6 latter and come up on an individual case-by-case basis or
7 topic-by-topic basis and more reflective, not directly in
8 toxicokinetics, but, you know, exposure duration. So it's
9 really not head on addressed as toxicokinetics, per se.

10 CHAIRPERSON FROINES: It's a major issue.

11 I would also caution you about the notion of
12 adverse effects. I would be careful to not come in and
13 state something shouldn't be done because it doesn't
14 constitute an adverse effect, because a change may have
15 physiologic implications that may result in adverse
16 effects. And so I think that one needs to look at the
17 issue broadly on that. That issue has come up here before
18 with this panel. Do you know what I mean?

19 PANEL MEMBER FUCALORO: You mean something may
20 not have a toxicological endpoint that anyone has seen,
21 but one has seen a biochemical change?

22 CHAIRPERSON FROINES: And those changes may have
23 implications for adverse effects.

24 PANEL MEMBER FUCALORO: They've not been
25 identified.

1 CHAIRPERSON FROINES: And maybe adverse effects
2 in and of themselves and we may not just know enough.

3 PANEL MEMBER FUCALORO: When you said it, I had a
4 sense of deja vu. I guess you've said it before.

5 CHAIRPERSON FROINES: No, I think Paul's raised
6 it before.

7 PANEL MEMBER FUCALORO: Well, someone has.

8 CHAIRPERSON FROINES: Paul.

9 PANEL MEMBER BLANC: I think that there was one
10 of their sections that was -- at least one of their
11 topics, I think, was trying to get at that which was 4B
12 Evaluating Clinical Signs and Symptoms in Humans versus
13 Animal Studies. I would just point out that it's very
14 difficult to elicit symptoms from an animal.

15 DR. PFEIFER: We understand that.

16 PANEL MEMBER BLANC: You may want to think about
17 how you word that as well. But I imagine that that was
18 part -- that's driving that section to some extent, I
19 suppose.

20 What John was just alluding to in terms of what
21 is the clinical correlation of a biochemical abnormality
22 perhaps, I don't know.

23 PANEL MEMBER BYUS: Again, I would like, John,
24 some clarification on what you would like Peter and I to
25 do with this document, because I was going to ask you this

1 and I appreciate you're input.

2 I mean do you want us to review it for the
3 science, particularly? Do you want us to review it -- I
4 mean, clearly that is the main point, but how editorial, I
5 guess, is the best word to use, do you want us to be or
6 should we be?

7 CHAIRPERSON FROINES: My concern is that I
8 want -- I need to reserve your independent evaluation of
9 their document. That's what we are required in a
10 statutory context, that we need to tell them whether we
11 think it's good or not, and that to over simplify it. And
12 to a degree that we begin to become -- play a staff role
13 and really work out the details of a document, I think we
14 begin to have -- it becomes more difficult to have an
15 independent evaluative position with respect to the
16 document.

17 So I would -- but at the same time, we've also
18 seen the lead as helping to facilitate the process. But I
19 think that one has to be a little careful about that so
20 that one doesn't get so deeply involved that you lose
21 one's independent function. So I would basically leave it
22 up to you and Pete's discretion, but I would suggest that
23 the most important place of review will be at the final
24 draft review. Although, I think one can give suggestions
25 along the way.

1 PANEL MEMBER FUCALORO: Especially, if they sense
2 things are going in the wrong direction, we certainly
3 don't want at the end their to be major changes. But if
4 they believe that there are problems, really significant
5 problems early on, I think it's important that they get
6 that information to the authors.

7 PANEL MEMBER WITSCHI: You know, I really would
8 like to side with you and see what you said. If memory
9 serves correctly, the whole thing started with a very
10 simple question. This was one of the risk assessments,
11 some data on cholinesterase inhibition and I've forgotten
12 what species were not considered to be other elements.

13 And the panel asked why not? And the answer was,
14 well, the EPA doesn't do it either or something along
15 those lines and this really triggered the whole workshop
16 and the whole symposium and the process.

17 And so clearly the panel eventually has to agree
18 with the conclusions which are being drawn from the
19 science. And I'm perfectly happy to draw some conclusions
20 from the science. I would be very uncomfortable to go
21 into all the detail, whether all the science is there or
22 not, because that's not my field of expertise.

23 But what I really would like to see eventually is
24 a document, that I have from -- I've seen so far, is going
25 to be a very good document.

1 But what I really want to see is a document which
2 spells out the issues, and you've come to some conclusions
3 and then our task is whether we can agree with those
4 conclusions.

5 CHAIRPERSON FROINES: I agree. I think it's --
6 I've said it twice, I don't want to repeat myself, but
7 it's important to preserve the independent evaluation of
8 the panel. It's also important to preserve the energy
9 level of the panel and both those things are significant,
10 especially given the fact the we had four and today is the
11 fifth meeting on SB 25, so people have been really dragged
12 through the mud in a sense in that effort.

13 PANEL MEMBER BLANC: Or drive through the
14 forests.

15 (Laughter.)

16 CHAIRPERSON FROINES: I'm not doing to well at
17 metaphors today.

18 And I'm assuming that since Paul Gosselin or
19 Keith haven't stood up and started to scream that this
20 notion of having a joint effort with OEHHA and DPR and
21 ourselves to find some of the external experts, so we can
22 all feel comfortable with that, is --

23 DR. PFEIFER: That's perfectly acceptable. I
24 mean, we're formulating a list based on people we know
25 professionally in this field. But there are others that

1 you may not know of who -- and the other question that's
2 come up, do we want to have each outside expert review
3 every paper or let them pick papers or, you know, that's
4 another question that I think we need to address.

5 CHAIRPERSON FROINES: Well, I would -- well,
6 that's not -- this is something we'll have to work on
7 together, because it's not a trivial issue, because on the
8 one hand you might say well, we would pick people based on
9 their expertise and who would be best at looking at a
10 particular issue. That's the easiest answer.

11 But at UCLA we have a Department of Pharmacology
12 with some people who have spent their lives on
13 acetylcholinesterase. And that they are not necessarily
14 toxicologists, but who they have such an incredible depth
15 of science, that they could look at the science without
16 necessarily knowing all the toxicology and look at your
17 document and give vital input to it. So that it seems to
18 me that who you actually ask to do the review is a
19 creative undertaking.

20 So I think the answer to the question is yes,
21 meaning, you know, it's to be worked out. It's an ongoing
22 process.

23 PANEL MEMBER WITSCHI: I would like to call your
24 attention to something that you probably don't know,
25 because it's very exotic. And this is in certain

1 aircraft, there are once in awhile leaks of hydraulic
2 fluid or engine oil into the cabin. And some of those
3 contain organophosphorous compounds in trace amounts, but
4 there is some concern out there among pilots and flight
5 attendants that this might represent a toxic hazard.

6 DR. PFEIFER: I would agree with that. And
7 there's also, as most of you may know, on international
8 flights going to like New Zealand, Australia and Jamaica,
9 they routinely either preboard or actually while the plane
10 is in flight, fumigate.

11 PANEL MEMBER WITSCHI: But those are the lights
12 they use. These are not organophosphorous compounds.

13 DR. PFEIFER: Oh, well, that's true. I don't
14 know. I really would kind of take exception to being
15 dosed while I'm going on vacation.

16 (Laughter.)

17 PANEL MEMBER FUCALORO: They have a sprinkler
18 system with malathion.

19 CHAIRPERSON FROINES: Well, see that's what the
20 Government has in mind when they started thinking about
21 this new way of doing human experiments. They're going to
22 use people on airlines as the study population.

23 CHAIRPERSON FROINES: Thank you very much. I
24 think we're finished for the moment, unless somebody else
25 on the panel has further comments?

1 And it's obviously an ongoing effort.

2 Congratulations.

3 DR. PFEIFER: George had a question.

4 DR. ALEXEEFF: I'll just ask my question. It
5 sounded like the way you -- because David had asked --
6 talked about the structure of the documents. It sound
7 like the panel, basically in the end, wanted one document
8 as opposed to one document with the science, another
9 document discussing the implications of the science, the
10 guidelines, it sounded like you wanted it more integrated.

11 PANEL MEMBER BLANC: Yes.

12 CHAIRPERSON FROINES: It's quite an undertaking.
13 Congratulations so far.

14 DR. PFEIFER: Thank you.

15 CHAIRPERSON FROINES: So we have a little bit of
16 time left. Maybe Andy can come back. But before Andy
17 comes back, I wanted to raise a question that hopefully
18 Peter -- Peter Witschi. Clearly, the situation has
19 changed since September 11th. Airlines have cut back
20 flights. There are significant security concerns. And
21 the panel had some difficulty, because there are three
22 people who are coming from Ontario, and United -- there
23 are no current nonstop flights from Ontario to San
24 Francisco anymore, strange as that may seem.

25 And so Craig and Roger and Tony had to go to

1 Oakland and take a cab across. And so that -- and when
2 they arrived, they were in less than a good mood, to say
3 the least.

4 And so the question for the panel is what shall
5 we do about location of meetings and travel, as we start
6 planning for next year?

7 PANEL MEMBER WITSCHI: Well, first of all, if
8 those guys are unhappy sitting in a cab across the bridge,
9 I'd encourage them to drive themselves.

10 PANEL MEMBER FRIEDMAN: That's even worse.

11 May I suggest that if we meet in the bay area --
12 when we meet in the bay area, that we meet in Oakland,
13 that would make their life a lot simpler and it's not that
14 hard for us to get over at least not for me.

15 CHAIRPERSON FROINES: Well, Gary, it's
16 interesting you say that, because I personally agree with
17 you, I like going into Oakland, but the one member who's
18 missing is Stan Glantz who hates the idea of having to go
19 to Oakland. So there's no unanimity. I don't what Paul's
20 position on this.

21 PANEL MEMBER FUCALORO: Is it because he's a
22 snob?

23 (Laughter.)

24 PANEL MEMBER BLANC: Well, I don't think that
25 there's any difference for -- any major difference between

1 if we're having a meeting, you know, at this location and
2 having a meeting at the Oakland Hyatt or whatever it is.
3 I think there have been times where we've had meetings at
4 UCSF itself, and those have been for logistical reasons
5 that would make it as hard to get here as to get to
6 Oakland, but those have been the exceptions rather than
7 rules.

8 But there have been one or two times meetings,
9 because neither Stan or I -- there was no way to come
10 otherwise because we had to be -- and you know we were
11 only there for part of the meeting.

12 CHAIRPERSON FROINES: Jim should join us, I
13 think.

14 But if we are in a situation like today, there
15 wouldn't have been any substantive difference for me to go
16 to Oakland or San Jose, if that would help and have people
17 fly in and out of San Jose.

18 CHAIRPERSON FROINES: But you're coming from
19 Davis, right?

20 PANEL MEMBER FRIEDMAN: I live up north and so it
21 would be difficult, very difficult.

22 PANEL MEMBER FUCALORO: San Jose is tough.
23 Oakland is --

24 PANEL MEMBER WITSCHI: What about Sacramento?

25 PANEL MEMBER BLANC: Yeah, Sacramento is a looser

1 for everybody.

2 PANEL MEMBER BYUS: Sacramento is another easy
3 one for us to fly in.

4 PANEL MEMBER BLANC: No, Sacramento is basically
5 your -- I mean, that's like two hours each way for -- I'd
6 rather go to Ontario than go to Sacramento.

7 PANEL MEMBER FUCALORO: Is that right?

8 CHAIRPERSON FROINES: You would?

9 PANEL MEMBER FRIEDMAN: It's a long drive.

10 CHAIRPERSON FROINES: You can fly to Sacramento.

11 PANEL MEMBER WITSCHI: You can take the train.

12 (Laughter.)

13 CHAIRPERSON FROINES: I have done it a number of
14 times.

15 PANEL MEMBER WITSCHI: You can take the train.
16 It's not bad, the train, actually.

17 PANEL MEMBER BLANC: I can drive to San Luis
18 Obispo and take the train to LA, too.

19 CHAIRPERSON FROINES: Now, the fact of the matter
20 is --

21 PANEL MEMBER FUCALORO: Oakland is the best.

22 CHAIRPERSON FROINES: Let me suggest something
23 that Paul may be forgetting, which is if Roger and Tony
24 and Craig couldn't get a nonstop flight from Ontario, that
25 probably means they can't get a nonstop flight to Ontario.

1 So when you say you'd just as soon go to Ontario, you're
2 not going to have a nonstop flight.

3 PANEL MEMBER BLANC: I can't get to Ontario and
4 back in the same day anyway, by and large. So I always
5 went down the evening before, if it was Ontario and then
6 just flew back.

7 But I mean the last time I looked at it -- from
8 here, I think that was the difference, in fact, is that
9 the first flight up --

10 PANEL MEMBER ATKINSON: There are no flights,
11 period.

12 PANEL MEMBER BLANC: No, but I'm saying in the
13 old days where there was a flight to San Francisco, there
14 was still never a flight early enough from San Francisco
15 to Ontario to go in the same day. And so whereas to LA --

16 CHAIRPERSON FROINES: So not to prolong this, so
17 what -- we clearly have a vote for Oakland is one option.

18 PANEL MEMBER BLANC: Then there's the more
19 generic thing, which is that there has been a traditional
20 commitment to alternate meetings between southern
21 California and northern California, not every other
22 meeting -- I mean, we've been doing it like -- we were
23 doing it two up here, one down there.

24 It seems like we sort of strayed into four up
25 here and one down there, instead of two up here and one

1 down there.

2 PANEL MEMBER FUCALORO: We noticed.

3 PANEL MEMBER BLANC: So I think that it's
4 certainly time for us to have a meeting in southern
5 California.

6 CHAIRPERSON FROINES: I think we should also
7 consider --

8 PANEL MEMBER BLANC: That would certainly make
9 their lives a lot easier.

10 CHAIRPERSON FROINES: -- trying to find a place
11 at USC perhaps at the medical school or someplace in that
12 vicinity, because then the people from Riverside can come
13 a distance, and the people from the westside, like me, can
14 come from a distance. But we should also clearly have
15 meetings over in the Riverside area as well.

16 PANEL MEMBER FUCALORO: Speaking of lights, it is
17 not quite a flight of fancy, but what is the legal
18 constraints or requirements regarding being physically in
19 the same room. I'm thinking of teleconferencing. Is that
20 completely off the wall or is it something we could
21 actually consider?

22 CHAIRPERSON FROINES: I don't know what the legal
23 constraints are. I don't think it's as good a way of
24 communicating as one --

25 PANEL MEMBER FUCALORO: It's not.

1 CHAIRPERSON FROINES: But if we could look at it
2 as an option -- I mean, we need to -- I think what we
3 would need to do would be to check into our various
4 institutions about the facilities that are --

5 PANEL MEMBER FUCALORO: I believe I have the
6 facilities. I think you guys do too, right?

7 PANEL MEMBER BLANC: UCSF certainly doesn't, not
8 even remotely.

9 PANEL MEMBER BYUS: There's new Internet
10 teleconferencing procedures now that are much more
11 inexpensive that you can actually do on your own computer
12 in your own office. I mean, it might be something to look
13 into. I mean for certain issues, I mean, for example,
14 like reviewing the findings today to meet a deadline. It
15 seems we're always having meetings to just review, to get
16 the findings out in a timely manner.

17 PANEL MEMBER FUCALORO: It seems to me the
18 legal --

19 PANEL MEMBER BYUS: That would be easy to do over
20 teleconferencing. You know, when an issue came up where
21 we didn't have to have a full meeting and fly everybody
22 all over to do something. I don't know about the legality
23 though.

24 PANEL MEMBER FUCALORO: The public has to somehow
25 be able to plug in, so to speak, I mean put a television

1 here or something.

2 CHAIRPERSON FROINES: So from what I here in this
3 meeting, Peter is in Sacramento, so there's some
4 advantages to him to stay and go to a meeting in
5 Sacramento. Some people said Sacramento is okay. Paul
6 doesn't care for it.

7 But what I'm hearing is that for the next few
8 months, we should be planning meetings in southern
9 California, to try to --

10 PANEL MEMBER FUCALORO: Well, I understand the
11 next two meetings --

12 CHAIRPERSON FROINES: -- to balance things out.
13 Oakland is an option, and that's probably all we have to
14 really decide at this particular moment.

15 PANEL MEMBER FRIEDMAN: Can I just pursue this a
16 little. Was the problem with the cab ride the Bay Bridge
17 traffic tie up? Is that why it was a problem to get over
18 here this morning, why you guys were in a bad mood?

19 (Laughter.)

20 PANEL MEMBER FUCALORO: Listen, the meeting was
21 at 10:00, right? We've been up for six hours by the time
22 the meeting started.

23 PANEL MEMBER FRIEDMAN: Oh, okay.

24 PANEL MEMBER FUCALORO: And there was no bad
25 traffic between Oakland and here. In fact, the traffic

1 was beautiful.

2 PANEL MEMBER FRIEDMAN: I was going to suggest
3 that BART was an alternative, because it picks you up at
4 the Oakland Airport, but that's not the problem. But when
5 we go to southern California, we often stay overnight, why
6 can't the same thing happen when people come up here?

7 PANEL MEMBER FUCALORO: That's a point. I'm an
8 honest man, I concede that that's a point.

9 CHAIRPERSON FROINES: I think we've gone as far
10 as we're going to go on this particular topic.

11 So it's only 1:25. Andy, do you want to try and
12 finish out?

13 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
14 SALMON: Can we take a five minute break?

15 CHAIRPERSON FROINES: If we can bring this as
16 close to closure, I think we will have done a good job.

17 (Thereupon a brief recess was taken.)

18 CHAIRPERSON FROINES: Everybody should note that
19 we are not going to vote on these chemicals today, because
20 we're going to try and get as far along as possible. And
21 one of the chemicals, carbon disulfide was not noticed, so
22 we couldn't take a vote anyway on carbon disulfide. So we
23 will finish this off and take a vote on a later date.

24 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
25 SALMON: Okay. So the next chemical that I'm going to

1 talk about is the methylene dianiline. The panel reviewed
2 the derivation in March and there's a couple of changes
3 we've made in response to comments by the panel. We more
4 accurately described the disease seen in humans and we
5 also made a point of mentioning the carcinogenicity.
6 We've adopted this as a principle now that when a
7 material, which is up for review for a chronic noncancer
8 REL, is also, in fact, a carcinogen on the hot spots
9 universe, that we should mention that in the REL summary.

10 We looked for evidence of any differential
11 effects on infants and children and basically found
12 nothing that gave us any indication.

13 So the endpoint is retinal toxicity. I mean, it
14 was a possibility that this would have a differential
15 effect, I suppose, since it's somewhat neurologically
16 related. But we don't really, I think, know enough even
17 about the mechanism to do anything other than speculate at
18 this point, so we have to stay with the defaults.

19 --o0o--

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

21 SALMON: The next one I want to present --

22 PANEL MEMBER BLANC: Can you just take note that
23 you need to correct your footer in the process.

24 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

25 SALMON: I'm sorry about that. Unfortunately, the wrong

1 section break got deleted when we were in the process of
2 -- thank you for pointing that out. I'm sorry. That is a
3 typographical error, and hopefully we will be presenting
4 phosphine in due course with a proper footer.

5 Selenium, again, this was one which the panel has
6 looked at previously. The complexity here is that we are
7 doing a root to root extrapolation. The critical effect
8 is the induction of symptoms of selenium and excess in
9 humans in dietary studies and epidemiological studies in,
10 I think, China.

11 And the concern was that it's possible to inhale
12 enough selenium possibly to induce similar symptoms by
13 this root. So what we have done is calculated an overall
14 intake based on the oral root using similar methodology to
15 the U.S. EPA's reference dose.

16 And then we have made a number of assumptions in
17 the root to root extrapolation, which we have clarified in
18 response to discussion at the last meeting.

19 The other thing we've done is looked at the
20 potential implications for children's health. And in this
21 case, the key study being basically environmental
22 epidemiological study does, in fact, include children as
23 young as one year old. There is also in the database on
24 the compound, a developmental study in hamsters. And so
25 we do have some reasonable basis in this case perhaps

1 uniquely for feeling that the chronic REL should be
2 protective of infants and children.

3 --o0o--

4 PANEL MEMBER FUCALORO: And, of course, the
5 inhalation REL is 20 micrograms of selenium itself,

6 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

7 SALMON: Yes, to the compounds, then the actual
8 gravimetric amount would be adjusted to --

9 PANEL MEMBER FUCALORO: Grams of selenium?

10 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

11 SALMON: Yes. That refers to selenium.

12 PANEL MEMBER ATKINSON: On the next page, I think
13 you should leave back in the vapor pressure of elemental
14 selenium, ten to the minus three. It's a rather important
15 number, because it means it's going to be at least
16 partially in the gas phase in the atmosphere.

17 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

18 SALMON: So we should not have deleted that.

19 PANEL MEMBER ATKINSON: So leave the one at 20
20 degree C and don't leave the one at 356, but leave the
21 selenium at zero.

22 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

23 SALMON: Okay.

24 CHAIRPERSON FROINES: Roger, what page are you
25 on?

1 PANEL MEMBER BLANC: The very first page.

2 PANEL MEMBER FUCALORO: A92.

3 PANEL MEMBER ATKINSON: And on A93, the first
4 sentence after, "Effects of human exposures," I think it
5 would be wise to delete the word "gas" after CO2. It
6 can't be a gas. It's got to be present in the particulate
7 phase.

8 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

9 SALMON: Yes. Okay.

10 PANEL MEMBER ATKINSON: I'll just throw another
11 one at you. You didn't make any consideration of
12 dimethylene selenide, which is volatilized bacterial or
13 microbial degradation of sulfur that leads to dimethyl
14 selenide. I don't know whether I'm really being facetious
15 or not, but it's probably present in the atmosphere in
16 some places.

17 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

18 SALMON: Yes, we're not -- I don't think we have any
19 evidence of it being an issue for the hot spots program,
20 but it's probably something that we should just check
21 because these things do have a habit of appearing in
22 strange places.

23 I mean, maybe we could ask whether anybody has
24 got a hot spots measurement on that near a sewage works or
25 something.

1 PANEL MEMBER ATKINSON: Well, the other place
2 would be if you're trying to bioremediate high levels of
3 selenium, you'll end up with dimethyl selenide.

4 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
5 SALMON: I'm not aware we have such a situation. We'll
6 check into that.

7 The next one that we're going to talk about is
8 sulfuric acid. And the panel reviewed this in some detail
9 back in March. And the issue here is how do we
10 accommodate the children's health impacts. The derivation
11 that we proposed for the REL has not changed.

12 However, there's extensive epidemiological work,
13 which interalia was reviewed by the air quality advisory
14 committee, the corresponding panel for the criteria
15 pollutants when they were looking at the criteria
16 pollutants for SB 25.

17 And they actually have reviewed a number of
18 epidemiological studies. It appears that the critical
19 exposure, which results in exacerbation of asthma in
20 children, is generally described as sulfate aerosol. But
21 an important component of that response appears to be
22 generic to acid aerosols of which obviously sulfate is a
23 large component in some situations where exposure to the
24 criteria pollutants is occurring.

25 But anyway, we felt that in view of this

1 important impact on children's health from sulfate
2 aerosols that we should review that evidence in relation
3 to our proposed chronic REL for sulfuric acid.

4 And one of the problems with the epidemiological
5 data is that it doesn't show a clear threshold for that
6 response. It sort of goes down, more or less, linearly
7 about to a level at which the effects disappears due to
8 sensitivity of the study as much as anything else.

9 But if there is -- the statement from the papers
10 and from the reviewers is that if there is a threshold,
11 it's probably something around two micrograms per meter
12 cubed. This is the general consensus as to where the
13 effects start.

14 And if taking that into account and taking into
15 account that we believe that the asthmatic children, the
16 most sensitive subpopulation that we're likely to have to
17 deal with in a hot spots situation, we feel that this
18 chronic REL, which was proposed on the basis of the animal
19 studies in nonhuman primates, the proposed REL of one
20 microgram per meter cubed is adequate in that it is
21 sufficient, just about, to protect asthmatic children.

22 And because they are a highly sensitive
23 subpopulation, we wouldn't expect to have a large safety
24 margin, but we feel that this is probably a case where the
25 proposed REL is appropriate.

1 PANEL MEMBER FUCALORO: You've mentioned this and
2 I just want -- it bears repeating it, at least to me, is
3 that you expect all atmospheric sulfuric acid pretty much
4 to be in aerosol form.

5 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

6 SALMON: Yes.

7 PANEL MEMBER FUCALORO: You don't expect it into
8 a gas form?

9 PANEL MEMBER ATKINSON: No.

10 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

11 SALMON: Not by the time --

12 PANEL MEMBER FUCALORO: Low pressure.

13 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

14 SALMON: Certainly not by the time it makes it over the
15 fence, and into the --

16 PANEL MEMBER FUCALORO: Yeah.

17 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

18 SALMON: One of the reasons why I wanted, you know, to
19 discuss this particular one with you and, you know, may be
20 get a little bit of feedback, is that we're looking at the
21 same database.

22 And at our proposed REL for nitric acid, which as
23 I mentioned earlier, we're not bringing forward as a
24 proposal at this point, and thinking that well, you know,
25 it's an acid which is probably going to be turning up in

1 aerosol form in the environment, as a result emissions of
2 nitric acid are indeed in nitrogen oxides from hot spots
3 sources.

4 And we would basically anticipate that the same
5 kind of constraints on what would be an acceptable
6 exposure for children that we've identified for the
7 sulfuric acid aerosols, is probably going to be -- it
8 would probably be reasonable to assume that we should
9 regard that as a limit for nitric acid aerosols, as well.
10 And in the case of the nitric acid proposal, partly
11 because, frankly, I think it's based on some older and
12 less exhaustive animal studies in terms of the critical
13 study.

14 That the nitric acid, the level we had originally
15 put forward in the draft would not be protective of
16 asthmatic children. So this is the reason why we pulled
17 this one back. And what we're thinking is that we need to
18 take account of this data on acid aerosols in relation to
19 the nitric acid.

20 PANEL MEMBER ATKINSON: Nitric acid can be
21 present in the gas phase quite easily. It's got a fairly
22 high vapor pressure. So unless there is something to
23 neutralize it, like ammonia, it will be present in the
24 atmosphere in the gas phase.

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: Well, I think this is a further reason why we
2 need to spend more time thinking about nitric acid.

3 But as a starting point, we feel we ought to look
4 at the impact of acid aerosols as possibly a constraint on
5 what would be acceptable as a chronic REL for nitric acid.

6 PANEL MEMBER ATKINSON: You just used the words
7 acid aerosol and nitric acid won't be present in on -- May
8 not be present.

9 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

10 SALMON: Depending on the nature of the emission.

11 PANEL MEMBER ATKINSON: Or on the other
12 components in the atmosphere.

13 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

14 SALMON: Yes. That's something that we should perhaps
15 consult with the Air Board as to exactly what's likely to
16 be out there.

17 PANEL MEMBER BLANC: This may have come up the
18 last time we discussed sulfuric acid, but the compound was
19 involved in a couple of big releases in the east bay,
20 which was a trisulfuric acid --

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: The olium.

23 PANEL MEMBER BLANC: Yes, olium breaks down to
24 sulfuric acid?

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: I think basically, by the time, it's been out in
2 the atmosphere and had a chance to react with a certain
3 amount of ambient moisture, it's reasonable to regard it
4 as being primarily the same as a sulfuric acid aerosol.

5 PANEL MEMBER BLANC: So in your major uses and
6 sources, given the historical importance of these oilium
7 releases, do you think you should have a sentence there
8 about oilium breakdown.

9 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

10 SALMON: Yes we will add that.

11 --o0o--

12 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

13 SALMON: And then the next item the --

14 PANEL MEMBER BLANC: One other question, I'm
15 sorry. Is there any release of sulfuric acid in natural
16 volcanic or thermal sources?

17 PANEL MEMBER ATKINSON: Yeah, it's released from
18 volcanoes.

19 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

20 SALMON: Volcanoes, certainly. I think the biggest
21 problem that I'm aware of from the sort of the geothermal
22 type of sources is, in fact, hydrogen sulfide to reduce
23 rather than to oxidize is safe. But certainly I think
24 there are plenty of circumstances when sulfur oxides
25 release from volcanic sources. The general ambient levels

1 of sulfur pollutants in California from both natural and
2 anthropogenic sources is fairly low.

3 I mean, in the criteria pollutant universe,
4 sulfur oxides are a large problem on the east coast due to
5 particulate.

6 PANEL MEMBER BLANC: Sulfur containing coal
7 burning.

8 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
9 SALMON: Sulfur containing coal into a somewhat lesser
10 containing fuel oil. Whereas, California has a habit of
11 using relatively low sulfur oil for diesel and fuel.

12 PANEL MEMBER ATKINSON: It might be good to add a
13 sentence or two right at the first page stating that any
14 sulfur oxides emitted into the atmosphere will end up
15 converted in that gas phase or through rain or cloud drops
16 into the sulfuric acid.

17 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
18 SALMON: Yes.

19 PANEL MEMBER BLANC: Well, because Mount Lassen
20 was, but not extinct actually.

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
22 SALMON: Clear, there's a possibility for episodic
23 excursions. It's not on a very large scale. I don't know
24 that we can regulate against them.

25 --o0o--

1 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

2 SALMON: Vinyl Acetate. This one was one in which the
3 panel hasn't looked at in detail in March. And so this
4 is -- here it is.

5 The proposed REL is based on historical lesions
6 of the nasal epithelium in rats, a long-term inhalation
7 study. There's an observed LOAEL end and an observed
8 NOAEL.

9 And we have calculated on this basis a proposed
10 REL of 50 parts per billion. And a fairly high quality
11 study in terms of the source data and not having to apply
12 too many uncertainty factors. And the human equivalents
13 concentration includes the RGDR calculations. And so the
14 additional intraspecies factors on top of that is three.

15 And we have included an intraspecies uncertainty
16 factor of ten for human diversity.

17 --o0o--

18 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

19 SALMON: The chronic REL here basically doesn't have any
20 very noticeable allowance for children's health. I think
21 the statement which we have in the summary is -- well, we
22 have this usual problem that we've got a somewhat irritant
23 related sort of endpoint, but no data on children.

24 But on the other hand, at least here we do have a
25 comparison REL, which is on a developmental study. So we

1 have a safety margin relative to that in the proposed REL.

2 And we are, for want of better information,
3 relying on the uncertainty factors, both of intraspecies
4 extrapolation and for the human intraspecies uncertainty
5 factor to species to conclude that the proposed chronic
6 REL would be sufficiently protective of children's health.

7 PANEL MEMBER BLANC: And the reason that you
8 couldn't use a benchmark approach was because the -- or
9 was it just too steep?

10 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

11 SALMON: Basically. Basically, it's too steep a dose
12 response to get a very clear analysis. The other problem
13 is just the way the data reported.

14 We have, at this point, a little bit of a problem
15 converting the -- this table where it's reported as very
16 slight, slight moderate, and severe, and then, you know,
17 the incidents of those different levels. That's a little
18 bit complicated to --

19 PANEL MEMBER BLANC: Translate.

20 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

21 SALMON: -- to actually translate into something where our
22 standard use of the benchmark doses software we expect a
23 single parameter input. Maybe this is something where we
24 need to, you know, think about how perhaps we could tackle
25 that in the future as a method development issue, but we

1 don't really have the technology to do that well at this
2 point.

3 CHAIRPERSON FROINES: Given where we are, there's
4 nothing to preclude the panel from adopting the chronic
5 RELs that you've presented today with the exception of
6 carbon disulfide. So that unless there are major
7 objections, it seems to me that we would cut down having
8 to take up the issue again for these compounds at a later
9 meeting if we did go ahead and vote. So what's the
10 motion?

11 PANEL MEMBER BLANC: The motion is bearing in
12 mind -- no, that's too wordy. Taking into account the
13 changes agreed to in the draft document, the panel
14 approves the specific chemicals presented, with the
15 exception of carbon disulfide.

16 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
17 SALMON: So it's the batch 2B chemicals that this motion
18 refers to, not the batch 2A chemicals?

19 PANEL MEMBER FUCALORO: Right.

20 CHAIRPERSON FROINES: Is there a problem, George?

21 DR. ALEXEEFF: No. I just thought you might want
22 to list the chemicals.

23 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

24 SALMON: It's shown on the slide.

25 DR. ALEXEEFF: And for the record, these Batch 2B

1 chemicals are acrylonitrile, beryllium, and compounds
2 chloropicrin, diethanolamine, ethylene dibromide,
3 isophorone, maleic anhydride, methyl isocyanate,
4 4,4-methylene dianiline, selenium and compounds other than
5 hydrogen selenide, sulfuric acid and vinyl acetate.

6 PANEL MEMBER FUCALORO: Is there a second for
7 that?

8 CHAIRPERSON FROINES: Are you seconding?

9 Discussion?

10 All those in favor?

11 (Hands raised)

12 CHAIRPERSON FROINES: Vote is unanimous. The
13 resolution is approved.

14 I should say that I think that vinyl acetate is
15 more likely to exert its toxicity through acid aldehyde,
16 but you guys don't agree with that. But I think vinyl
17 acetate is more probable, is more benign.

18 So, Andy, you have one more slide, which is where
19 do we go from here. And if you can do it in five minutes,
20 we can --

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: I trust I can do it considerably faster than
23 that.

24 So I'm just making sure I've got the right one.
25 Okay, so the next steps for the chronic RELs. Well, we

1 have completed 2B, but we still have the 2A compound which
2 we will bring -- we will notice and bring to your
3 attention at the next meeting for appropriate, further
4 instruction and or resolution.

5 We now have batched three. We have a second
6 draft, which has yet to go through the public comment
7 process. So we will be releasing the second draft for the
8 period of notice and public comment, and also, of course,
9 sending it to the panel in due course.

10 When we send it to the panel, we will include the
11 public comments and the response -- our response to those
12 comments.

13 And then the panel will, I assume, want to review
14 the Batch three chemicals in groups of not more than about
15 15 or 20 at a time.

16 It may be that the batches are a little smaller
17 than that, because there are some materials in batch 3
18 which, quite frankly, I don't think we're going to propose
19 a REL for, because there is our further investigation that
20 identified an either no-use in California or
21 no-significant hot spots toxicity issues.

22 So I think for those things for which there is
23 absolutely no use in California identified, I think we
24 will probably not be bothering you with those ones. But
25 there are, in fact, a couple of interesting chemicals in

1 there as well, so I hope it won't be too distressingly
2 boring.

3 PANEL MEMBER BLANC: Thank you.

4 CHAIRPERSON FROINES: Thank you. Do we have a
5 list of these chemicals, at this point, because we'll need
6 to assign them?

7 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

8 SALMON: I will Email you a list -- the list which, you
9 know, is potentially out there is the same as the first
10 public comment draft list of things remaining. But as I
11 say, we need to actually go through the list and review
12 some of them before we have it absolutely finalized.

13 So what I can do is I can Email you the list as
14 soon as we have it, which should be fairly soon.

15 CHAIRPERSON FROINES: So Email me the list and
16 I'll take a resolution to close the meeting, before people
17 walk out of the room.

18 PANEL MEMBER FUCALORO: Second.

19 CHAIRPERSON FROINES: We need to vote.

20 PANEL MEMBER BLANC: All in favor?

21 (Ayes.).

22 CHAIRPERSON FROINES: Congratulations, we did the
23 entire agenda, and we're early.

24

25

1 (Thereupon the California Air Resources
2 Board, Scientific Review Panel
3 was adjourned at 2:00 p.m.)
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CERTIFICATE OF REPORTER

I, JAMES F. PETERS, a Certified Shorthand Reporter of the State of California, and Registered Professional Reporter, do hereby certify:

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

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

IN WITNESS WHEREOF, I have hereunto set my hand this 13th day of December, 2001.

JAMES F. PETERS, CSR, RPR
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