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

MILBERRY CONFERENCE CENTER
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
500 PARNASSUS AVENUE
SAN FRANCISCO, CALIFORNIA

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APPEARANCES

MEMBERS PRESENT:

- Dr. John Froines, Chairman
- Dr. Roger Atkinson
- Dr. Paul D. Blanc
- Dr. Craig Byus
- Dr. Gary Friedman
- Dr. Anthony Fucaloro
- Dr. Stanton Glantz
- Dr. Peter S. Kennedy
- Dr. Hanspeter Witschi

REPRESENTING THE CALIFORNIA AIR RESOURCES BOARD:

- Mr. Jim Behrmann, Manager
- Mr. Bill Lockett, Deputy Ombudsman, Northern California
- Mr. Peter Mathews, Office of the Ombudsman

REPRESENTING THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT:

- Dr. George Alexeeff, Deputy Director for Scientific Affairs
- Dr. James Collins, Staff Toxicologist
- Dr. Melanie Marty, Senior Toxicologist
- Dr. Andrew Salmon, Chief, Air Toxicology and Risk Assessment

REPRESENTING THE DEPARTMENT OF PESTICIDE REGULATION:

- Mr. Paul Gosselin, Assistant Director
- Dr. Andrew Rubin, Staff Toxicologist

ALSO PRESENT:

- Ms. Elinor Fanning, UC Berkeley

	INDEX	PAGE
1		
2	AGENDA ITEMS:	
3	1 Continuation of Consideration of Draft Report:	1
4	Air Toxics Hot Spots Program Risk Assessment	
5	Guidelines, Part III: "Technical Support	
	Document for Determination of Noncancer Chronic	
	Reference Exposure Levels"	
6	2 Update to the Scientific Review Panel on the	22
7	Air Toxics Hot Spots Program Risk Assessment	
	Guidelines	
8	3 Discussion of Possible Topics for Future	39
9	"Pesticides in the Air" Panel Workshops	
10	4 Continuation of Consideration of Draft Report:	55
	"The Evaluation of Methyl Isothiocyanate (MITC)	
	as a Toxic Air Contaminant	
11	Adjournment	162
12	Certificate of Reporter	163
13		
14		
15		
16		
17		
18		
19		
20		
21		
22		
23		
24		
25		

1 P R O C E E D I N G S

2 CHAIRMAN FROINES: Welcome, everybody.

3 This panel has had approximately a two-month
4 break, so that everybody should be really raring to go.

5 Melanie doesn't want to hear that.

6 DR. GLANTZ: I just thought of a wise crack, but I
7 won't make it.

8 CHAIRMAN FROINES: The first item, there's no
9 other information I think that's particularly relevant at
10 the beginning, so we might as well just go right into the
11 agenda.

12 So we're going to continue to consider the draft
13 report, 23 of the first 43 compounds.

14 DR. MARTY: I'm Melanie Marty from the Office of
15 Environmental Health Hazard Assessment, and we're going to
16 present today the revisions made to the document based on
17 the panel's comments from the last three meetings or so.

18 Today we're talking about the technical support
19 Document for the determination of chronic reference exposure
20 levels for airborne toxicants.

21 This slide presents the definition of the chronic
22 REL. Essentially the chronic REL is the concentration in
23 air at or below which no adverse health impacts are
24 anticipated following long-term exposure. It is meant to
25 protect most people, including sensitive individuals,

1 although we are obviously unable to account for
2 idiosyncratic responses.

3 Exceedance of this REL does not necessarily result
4 in adverse health consequences, until you reach a high
5 enough level to see adverse health connections. I think
6 that's important that people understand that.

7 We made a number of revisions in the document.
8 This slide summarizes the revisions in the introduction.

9 We changed the uncertainty factor for interspecies
10 extrapolation when you're using primate data to three from
11 ten. This was based on comments from the panel that they
12 felt primates were close enough to people that perhaps we
13 shouldn't have lumped them together with rodents.

14 We added a brief discussion of hyperplasia as a
15 toxicological endpoint. That's on page 17 of the
16 introduction.

17 We also reworded our discussion of the benchmark
18 concentration approach on page 19 and in particular talked
19 about the difference between how US EPA does benchmark
20 concentration and how we have proposed to use it.

21 The difference being primarily that they are
22 looking for a benchmark which is the 95 percent lower
23 confidence limit on the dose that produces a ten percent
24 response rate. We felt that was closer to a LOAEL rather
25 than a NOAEL. We would rather use the 95 percent lower

1 confidence limit on the dose that produces a five percent
2 response rate. So that's one difference between our
3 approach and their approach.

4 We added an equation for unit conversion from ppm
5 to milligrams per cubic meter. That's on page 30.

6 We also on page 30 clarified our discussion of the
7 use of US EPA RfCs. Essentially what we have stated is that
8 we have evaluated the US EPA RfCs. In many cases we agree
9 with the choice of the key study, but we have somewhat
10 different approaches to the use of uncertainty factors and
11 we're also more consistent with what we describe as a
12 chronic toxicological study. So we actually have criteria
13 for the duration of the exposure.

14 We also made a number of generic revisions to the
15 toxicity summaries in the RELs. We responded to all the
16 panel members' comments.

17 We added emissions information from the air toxics
18 emissions database, which is the Air Toxics Hot Spot
19 Program's database of emissions reported by the air
20 districts and facilities.

21 We also added, where available, ambient
22 concentration data, which we intend to update to whatever we
23 can -- the latest year from the Air Resources Board. I
24 doubt they have their '99 all pulled together, but at least
25 we'll get the '98 emissions in. I'm sorry. In '98, the

1 ambient concentration data.

2 We added more description of key studies, and that
3 was in response to most of the panel members' concerns about
4 us not describing enough the information that was available.

5 We added comparison reference exposure levels
6 where you could have chosen one study or another with some
7 discussion of why the study we chose we chose.

8 We also added a section, strengths and limitations
9 of the data, and essentially organized some material that
10 was already in there into that section so it was easy to
11 find and describe, and we bolstered that section in a number
12 of cases.

13 The panel had directed us to go back and look at
14 our US EPA RfCs that we proposed just adopting. So we did
15 do that. And in fact with a number of the studies we agreed
16 with the choice of the study made by US EPA, but we would
17 have applied different uncertainty factors.

18 One of the things we did was drop the modifying
19 factor that EPA uses in a number of their RfCs. This
20 changed the chronic REL for ammonia, EGME, mercury and MTBE.
21 In general it went up, because they added an additional
22 modifying factor of three, which they of course divide
23 through by. And we removed that modifying factor so the
24 numbers went up a little bit. With rounding it ends up
25 being about a twofold, depending on the numbers.

1 In the case of mercury, we actually used different
2 uncertainty factors than US EPA. We dropped the modifying
3 factor, but we actually used a different uncertainty factor
4 so the number changes, it actually drops.

5 DR. FUCALORO: Can I ask a question? How does
6 three round to two? I'm not quite sure.

7 DR. MARTY: If you go through the calculation and
8 then round the final number, we rounded it to one
9 significant figure, so it ends up if you do the calculation
10 and round the final numbers, the difference isn't quite
11 three.

12 DR. SALMON: Like ammonia was 70 and 210. Went
13 from 70 to 210, so we rounded 70 up and 210 down.

14 DR. MARTY: Other changes --

15 DR. GLANTZ: Where is the limitations section?

16 DR. MARTY: It's section 7 of each toxicity
17 summary.

18 DR. GLANTZ: Okay.

19 DR. MARTY: I'm sorry. It's not in the
20 introduction. The last section, before the references.

21 DR. GLANTZ: I see them.

22 DR. MARTY: Other changes that were made in
23 response to our re-review of some of these issues, for
24 chlorine we used a benchmark concentration approach. This
25 approach we discussed quite a bit and essentially most

1 everyone agrees it's better than just using the NOAEL, LOAEL
2 divided by uncertainty factors approach.

3 In so doing, the reference exposure level changed
4 from .06 to .2 micrograms per cubic meter, and we did use a
5 benchmark concentration for a five percent response rate.

6 In the case of ethylene glycol monoethyl ether,
7 we actually read some studies that were suggested by
8 Dr. Blanc. They were human studies. They indicated to us
9 that the interspecies uncertainty factor should really be
10 higher than what we had initially proposed. So this dropped
11 the reference exposure level to 70 micrograms per cubic
12 meter.

13 The original number was an EPA RfC. We used the
14 same study and kept the key study, but rather than using an
15 interspecies uncertainty factor of three, we used ten, even
16 though we had a human equivalent concentration adjustment.
17 And that's basically as a result of us evaluating a series
18 of studies by Welch and Cohn, which couldn't themselves be
19 used because of uncertainties in the information, but
20 indicated that humans might actually be pretty sensitive to
21 the reproductive toxicology effects.

22 Ethylbenzene is another chemical that was
23 suggested we go back and look at the new chronic NTP
24 bioassay, which came out in the middle of last year. We did
25 that and revised the REL using that study. And the REL

1 changed from .2 to .4 parts per billion. The original
2 proposed REL was an EPA RfC based on developmental toxicity.

3 If we had used the EPA study and done our
4 methodology, we actually would have had an even higher
5 number. So we're not uncomfortable that -- we think we're
6 protecting against developmental effects.

7 In the formaldehyde summary we added a table with
8 comparisons of the REL, which was based on a human study to
9 RELs based on 13 animal studies. And essentially they
10 bracket that human REL. Some of them are lower, some are
11 higher. So it just strengthens the argument for the use of
12 those studies.

13 For hydrogen chloride we updated the RGDR from
14 what was originally in the document. Originally we proposed
15 to use an EPA RfC and, when we evaluated it, the RGDR was
16 changed and we also changed the low observed adverse effect
17 level uncertainty factor from ten to three in the process,
18 so the REL changed from seven to nine micrograms per cubic
19 meter.

20 In the case of methyl ethyl ketone, we went back
21 and looked at a study which I believe Dr. Blanc had
22 suggested us to look at it.

23 Mitran et al, 1997, is a study of exposed cable
24 factory workers and we replaced the rat study which we had
25 used, which in essence was actually a subchronic study. And

1 the REL changed. It actually dropped from 10,000 to 500
2 micrograms per cubic meter. So this was a significant
3 change and we were impressed by that and thought it would
4 have been much better to use that human study in this case.

5 In this case these workers were only exposed to
6 MEK. They did not have other solid exposures, and the
7 exposure assessment seemed to be relatively good for a human
8 study.

9 DR. FUCALORO: Curiosity on that, I mean, that's a
10 20 to 1 change. Now, the US EPA has any data? I mean, how
11 did they handle methyl ethyl ketone? I mean, something is
12 that big a change, I mean it's -- you have to understand
13 what that -- what other people think of that change.

14 DR. MARTY: The RfC for methyl ethyl ketone that
15 was developed by EPA in '92 has been withdrawn, and we
16 don't -- they don't have any number.

17 DR. FUCALORO: What was theirs and why was it
18 withdraw, by the way?

19 DR. MARTY: I think the methodology changed
20 between when they had developed it.

21 The original study that we proposed for the REL
22 was a rat study with whole body inhalation for 90 days, and
23 the toxic endpoint noted was increased liver weight and
24 relative kidney weight in the male and female rats.

25 In contrast this Mitran et al study, which looked

1 at people, was looking at neurotoxic endpoints. They had a
2 battery of neurobehavioral tests which obviously has some --
3 there are problems in interpretation of those tests, but in
4 addition they conducted motor nerve conduction velocity
5 tests, which are not subjective, at least near to the degree
6 that the neurobehavioral battery tests are. And they got
7 significant decreases in measured nerve conduction velocity
8 in three nerves.

9 So we felt that that was important information.
10 The Cavender study really didn't look at neurotoxicities, so
11 they have been missing the more important endpoint in this
12 case.

13 CHAIRMAN FROINES: I'm sorry. Where is that
14 described?

15 DR. MARTY: Page A-182, methyl ethyl ketone
16 derivation of chronic reference exposure levels.

17 And then the Mitran study is described on page
18 180.

19 CHAIRMAN FROINES: I'm sorry, Melanie, which is
20 the study with the nerve conduction velocity change?

21 DR. MARTY: That was Mitran et al, 1997. It's
22 described under effects of human exposure on page A-180.

23 These were relatively long-term exposures. The
24 average length of exposure was 14 years.

25 CHAIRMAN FROINES: Did they control for alcohol?

1 DR. MARTY: Jim is looking at the study.

2 They did have 41 exposed workers and 63 controls,
3 which they say were matched for age, physical effort at
4 work, work shift and socioeconomic factors.

5 I'm not sure that they specifically addressed
6 alcohol. You would have to assume, though, that the alcohol
7 usage was different in the 41 subjects and 63 controls if it
8 were to impact the results.

9 CHAIRMAN FROINES: The historical problem with
10 neurobehavioral occupational studies is always this problem
11 of alcohol, not controlling for alcohol consumption.

12 DR. SALMON: That isn't such a big problem now
13 with the neuroconduction velocities studies.

14 CHAIRMAN FROINES: I understand.

15 DR. SALMON: Which was one of the reasons why we
16 focused on that endpoint rather than the neurobehavioral
17 studies, because, as you correctly point out, the number of
18 variables and confounding factors which need to be taken
19 care of.

20 CHAIRMAN FROINES: It's also true that hexane
21 produces a distal axonopathy, as you know, and that myelin
22 changes are a late stage of that process, and so motor nerve
23 conduction velocity changes are in fact late stage change in
24 hexane exposures. So it may be that because you've got 14
25 years' exposure, you've got myelin damage as well as axonal

1 damage. That's the assumption, I assume.

2 DR. MARTY: Yes.

3 CHAIRMAN FROINES: Tony, question?

4 DR. FUCALORO: No, I'm done.

5 DR. MARTY: In the case of PGME, we originally
6 used a subchronic study for the REL, and there was a
7 submission to us from industry of a chronic toxicity
8 oncogenicity, two-year bioassay, that we read and have
9 incorporated into the document. And the result is that we
10 used it as the basis of REL rather than the subchronic
11 study, and the result is that the REL went from 0.6 to 2
12 ppm.

13 CHAIRMAN FROINES: The record should show that
14 Dr. Friedman is here now.

15 DR. COLLINS: The original study was subchronic
16 and the new study was chronic.

17 DR. MARTY: Correct.

18 For phosphoric acid we originally had an EPA
19 number which was based on a benchmark concentration, but the
20 benchmark concentration used again the 95 percent lower
21 confidence limit on the dose for ten percent response rate.
22 We went back and calculated that using the LCL on a five
23 percent response rate. The result was the REL changed from
24 10 to 7 micrograms per cubic meter.

25 That's it for the changes to the document.

1 I did want to -- maybe I should wait if there are
2 any questions.

3 I did want to talk about the next steps for this
4 document to clarify that, at least what we're thinking.

5 Okay. We will --

6 CHAIRMAN FROINES: The panel sees this as our rock
7 of Sisyphus, you know.

8 DR. GLANTZ: What's the rock of Sisyphus?

9 DR. BYUS: It keeps rolling. Roll it up there and
10 it comes back down.

11 CHAIRMAN FROINES: Who was condemned to roll the
12 rock up the hill, he gets it to the top of the hill, it
13 rolls back down, and he has to start over again.

14 And the chronic REL document has some of the
15 qualities of that.

16 DR. GLANTZ: I was actually going to speak to
17 that, but not as eloquently.

18 DR. MARTY: We need to incorporate any additional
19 comments that we get from the panel today and finalize the
20 methodology section and these first 23 chemicals.

21 We will then address the rest of the first batch
22 at the March 7th SRP meeting, so the panel will be receiving
23 the last 16 of the first 40 chemicals and with changes that
24 we have made pursuant to all the comments that has gone on
25 for the last three meetings. So you should be receiving

1 that very shortly.

2 CHAIRMAN FROINES: Help me. This next 16 are
3 chemicals that we have already discussed, you've made
4 changes?

5 DR. MARTY: Correct.

6 CHAIRMAN FROINES: And then they'll be coming back
7 to us again?

8 DR. MARTY: Correct. Just like this first 23. We
9 wanted to get all 40 to you, but December got in the way.

10 DR. GLANTZ: I had asked Melanie about this before
11 the meeting, why we didn't just get all 40 back, and I was
12 told that, as she just said, that they just didn't have time
13 to integrate the comments from the last meeting.

14 So what I would like to suggest is that subject to
15 any further discussion we approve the document as it's
16 before us, which is a method, a basic methodology in the
17 first 23, and then the rest of the 16 or 17 that they didn't
18 get to will just come in and maybe be incorporated as an
19 addendum, but appropriate of the rock of Sisyphus, I'd like to
20 approve this document.

21 And unless people have -- I read through it. I
22 thought it was fine.

23 And so the subsequent chemicals that we will deal
24 with would be treated as additions to an approved document,
25 rather than hold the document up. Because this is going to

1 go on for a long time as we add more and more compounds.

2 CHAIRMAN FROINES: We have 80 more to go.

3 DR. GLANTZ: Yeah. But I'd like to have this be
4 finished and approved so they have a finalized document and
5 then we'll just add chemicals to it.

6 CHAIRMAN FROINES: Do you want us to then take up
7 the 16 at a subsequent meeting?

8 DR. GLANTZ: Yeah. I mean, what she just said is
9 that they'll bring the rest of those back to us at the next
10 meeting, and I would expect that since they were discussed
11 at length already, hopefully it will be like -- at least
12 when I reviewed the document, I looked at it and said, yes,
13 they made the changes we suggested. I couldn't think of
14 anything else, so I'd like to approve it, unless someone
15 else found anything they wanted to do.

16 Then as the additional chemicals come, the next 16
17 we would take, approve unless there's still a problem, and
18 that would be treated as an addendum to this document. But
19 this document would be done and then the third batch or the
20 second batch and the third batch, as those come to the
21 committee and are discussed and dealt with would simply be
22 added to the approved document, rather than have the
23 document continue to wait.

24 CHAIRMAN FROINES: So you're basically proposing a
25 two-vote sequence?

1 DR. GLANTZ: Well, I'm proposing that we vote,
2 unless people have objections to it. I have no concerns
3 remaining with this document. That we approve this and
4 finalize it. And then as additional chemicals come to us,
5 that when those are approved they be added to the approved
6 document, rather than holding the document until all 120 or
7 however many there are compounds that will be dealt with.

8 CHAIRMAN FROINES: Comments on that?

9 DR. FUCALORO: I have no problem. There are a few
10 things that almost fall into the category of typos that I
11 can talk to her later about.

12 DR. GLANTZ: If other people have problems, then,
13 fine, but I don't personally have any problems with the
14 document as it stands now. If they do, they should be dealt
15 with.

16 DR. WITSCHI: I have a question about the future
17 of this document. What's the mechanism or the process? If
18 new data become available, which should be used to modify
19 what's already in it, because, you know, I've seen a few
20 examples where like this 1999 stuff which you didn't have
21 the last time, so as things -- if we approve it, you know,
22 as times move along, what's the mechanism to take care of
23 new developments?

24 DR. MARTY: We intend to keep relooking at these
25 chemicals as time goes on, for that very reason. There are,

1 as you pointed out, a number of examples in here where we
2 found new studies.

3 DR. WITSCHI: Yes. Will you bring those changes
4 before us?

5 DR. MARTY: Yes. We have to bring the chemicals
6 and the revisions before the panel.

7 CHAIRMAN FROINES: I guess I would suggest that if
8 you are going to make revisions that you make the revisions
9 over a period of time and bring as a block of chemicals.
10 The last thing I think we want to see is a chemical
11 dribbling in here and there.

12 DR. COLLINS: Chemical of the month problem.

13 DR. GLANTZ: Could be the pebble of Sisyphus.

14 DR. MARTY: That makes a lot of sense to us too.
15 Bring it in batches.

16 CHAIRMAN FROINES: I think that this then it does
17 begin to feel like an endless process.

18 DR. WITSCHI: Won't it give some mandate to them
19 to -- OEHHA gives us an update every year, every two years,
20 something like this.

21 DR. COLLINS: An annual update.

22 DR. WITSCHI: At one of the meetings.

23 CHAIRMAN FROINES: That make sense? That's good.

24 So, Melanie, I think you're still -- this is a
25 little bit -- should have come at the end of your

1 presentation rather than here, so why don't you go ahead.

2 DR. MARTY: Okay.

3 CHAIRMAN FROINES: Unless you are finished.

4 DR. COLLINS: We have no objection.

5 DR. GLANTZ: I actually thought she was finished.

6 I'm sorry.

7 CHAIRMAN FROINES: No, no.

8 DR. MARTY: I'm almost finished. I have four more

9 bullets.

10 As Stan noted, I talked to him a little earlier,
11 we wanted to address the rest of the first batch on March
12 7th, and then I think it's a great idea to have that added
13 as addendum.

14 We have to review the public comments on the
15 second batch of 40. We started that process, but we need to
16 keep going and make changes to those second batch of 40
17 based on the public comments, and also on the panel's
18 comments from the last several meetings. So in other words
19 all the things that we changed in these chemicals, we've got
20 to go back to the second batch and make those similar
21 changes. And then we were hoping to bring them to the panel
22 for review in June.

23 Then we have the third batch which has not even
24 gone out for the second public comment period yet, so that's
25 down the line.

1 CHAIRMAN FROINES: Now, the panel may not remember
2 this, but the chemicals have been assigned to the various
3 members of the panel. And I guess I'll ask Peter to make
4 sure everybody has that so they're reminded.

5 DR. GLANTZ: Why don't you give them, since some
6 of us have short memory, I guess -- no jokes, I'm sorry. He
7 can just give them to me again.

8 This is the current set. Okay. I can remember
9 this. I was going to say, as we get -- you haven't assigned
10 the second or third batch, have you?

11 CHAIRMAN FROINES: The second are assigned.

12 DR. GLANTZ: I thought my memory had completely --

13 CHAIRMAN FROINES: The second are assigned.

14 DR. GLANTZ: The second are. Okay. Maybe what
15 you should do is when we get the report from OEHHA on the
16 second batch, maybe you should send the assignments around.

17 CHAIRMAN FROINES: I'll redo it.

18 Peter or Jim, we've sent the assignments out, but
19 let's redo it.

20 DR. GLANTZ: For the second batch.

21 CHAIRMAN FROINES: For the second batch.

22 DR. GLANTZ: Why didn't you send that out
23 concurrently when you send the second batch out.

24 DR. MARTY: Okay. That's it for talking about
25 this document.

1 I have three more overheads, but it's actually
2 going to the second agenda item.

3 DR. GLANTZ: Let's finish with this before we go
4 on.

5 CHAIRMAN FROINES: You're moving -- the last
6 overheads are for the second agenda item?

7 DR. MARTY: Yes. These last three are really the
8 second agenda item, updating the panel as to where the rest
9 of all the hot spots guidelines are.

10 DR. GLANTZ: Let's finish this.

11 CHAIRMAN FROINES: In that second -- we had talked
12 on the telephone about you're talking about the implications
13 of what we've all done and that's what's coming?

14 DR. MARTY: That we should do now. That we should
15 do now.

16 What's coming is where is Part 4, where is part 5
17 in the process.

18 CHAIRMAN FROINES: No. But I mean these three
19 overheads.

20 DR. MARTY: Yeah. That's basically what else we
21 have to do for the Air Toxics Hot Spots Risk Assessment
22 Guidelines, but it's not the discussion of how you use the
23 numbers in this.

24 CHAIRMAN FROINES: Let's follow Stan's -- let's go
25 to Stan. Does that make sense?

1 DR. MARTY: Yes.

2 Unless you wanted to talk about issues of the
3 hazard index approach and how we used the numbers, some
4 issues have come up with the panel.

5 CHAIRMAN FROINES: Let's -- but that doesn't -- we
6 can have a discussion after we've actually approved the
7 document.

8 DR. MARTY: That's fine.

9 CHAIRMAN FROINES: Let's do that. So I guess the
10 thing to do is to ask panel members if they have comments on
11 anything that's been presented or changes that have been
12 made.

13 Let's start out with Stan.

14 DR. GLANTZ: No, I'm happy with the document.

15 CHAIRMAN FROINES: Gary.

16 DR. FRIEDMAN: I have no suggestions.

17 CHAIRMAN FROINES: Peter.

18 DR. WITSCHI: No problems.

19 DR. ATKINSON: I have three minor changes on the
20 physical and chemical properties, if I can just give you
21 those.

22 DR. BYUS: That's fine. Very good.

23 DR. FUCALORO: I have some changes, but they're
24 minor.

25 DR. GLANTZ: Just for the record, these changes

1 that Roger and Anthony mentioned, those are just minor
2 editorial corrections, there's nothing substantive; is that
3 correct?

4 DR. ATKINSON: There is a wrong vapor pressure in
5 one of them.

6 DR. FUCALORO: There's one -- is that
7 formaldehyde?

8 DR. ATKINSON: Yeah.

9 DR. FUCALORO: Formaldehyde is clearly wrong and
10 the number hasn't changed.

11 DR. ATKINSON: Yeah.

12 DR. FUCALORO: Other than that, they're mostly
13 typos.

14 DR. ATKINSON: Typos.

15 DR. GLANTZ: Well, then, I'd like to move that we
16 approve this document and finalize this document.

17 DR. KENNEDY: Second.

18 CHAIRMAN FROINES: Is there any further
19 discussion?

20 Then all in favor.

21 (Show of hands.)

22 DR. GLANTZ: It's unanimous.

23 CHAIRMAN FROINES: So the rock is tilting, holding
24 in place.

25 DR. MARTY: Okay. The next --

1 DR. GLANTZ: This is, by the way, a very nice
2 piece of work. And I think it continues the very
3 high-quality work that you guys have brought before us,
4 after we make you suffer appropriately. But it is very very
5 well done and it's just a massive undertaking.

6 DR. MARTY: That it is.

7 DR. GLANTZ: Very well done.

8 CHAIRMAN FROINES: I also think the panel gets
9 credit, though, for having been very thorough in their
10 review of this. That's been, I think, important so that the
11 public has trust in the deliberation that results in these
12 numbers being solidified.

13 Why don't you tell us what the meaning of all this
14 is.

15 DR. MARTY: I can go through these slides and that
16 will help focus that discussion.

17 Basically what we just approved today was Part 3,
18 the determination of chronic reference exposure levels. And
19 we will, as the discussion reflects, be adding chemicals as
20 we move along in over time.

21 We also have -- Judy, can I have the next slide.

22 As we just discussed Part 3, what we're going to
23 be doing, Part 4 is the technical support document for
24 exposure assessment and stochastic analysis.

25 And Dr. Glantz is the lead on that document. He

1 has received a copy and is plowing through it now.

2 The panel will receive the document mid February,
3 along with our responses to the comments. The public
4 comment period occurred a couple of years ago and then the
5 document sort of got -- well, we lost a lot of staff and
6 diesel exhaust got in the way. So we are now getting back
7 to the -- we responded to the comments. Everything is ready
8 to go, but we didn't want to give it to you before this
9 meeting to avoid a paper blizzard.

10 We intend to make an overview presentation of the
11 document and some discussion of the changes that were made
12 since the last version, which was presented by OEHHA to the
13 panel in March of, I think it was 1997.

14 So we had an overview of the document already
15 given to the panel. There was some discussion at that
16 meeting. And then we have made quite a few changes since
17 then to that document, so we'd like to just re-present the
18 document and talk about some of the key changes.

19 And then we anticipate that by the time the May
20 meeting rolls around the panel will have had enough time to
21 look at the document and we can start discussion by the
22 panel.

23 CHAIRMAN FROINES: In March?

24 DR. MARTY: In May. March 7 we'll present an
25 overview, but you folks will only have had the document a

1 couple of weeks at that point.

2 DR. GLANTZ: We're not meeting in April?

3 DR. MARTY: I don't know. I looked at my latest
4 notes indicating no April meeting. So that I'm just
5 throwing May out there, because I didn't realize there was
6 an April meeting.

7 CHAIRMAN FROINES: Jim.

8 MR. BEHRMANN: The next meeting date beyond March
9 has not been set yet.

10 DR. GLANTZ: I would think, I mean, I'm about a
11 half, a third, or halfway through the revised document, and
12 I would think that it could be discussed. I think it's a
13 long, complicated document, but it's, I think if there's a
14 presentation in the March meeting, then it would be
15 reasonable to have a discussion in the May meeting or rather
16 at the next meeting, whether it's in April or May.

17 I think that there have been a lot of changes to
18 the document. This is the one where they're trying to model
19 population variability, and rather than looking at single
20 numbers, take into account variability of breathing rates,
21 variability of how much dirt you eat, all of that sort of
22 variability, weather conditions, and there are a lot of, you
23 may recall, political problems with the document before
24 where there was some modeling going on, and as far as I am
25 able to detect it's now back to being based on science.

1 And but I have not had a chance to go through the
2 public comments. And I was just looking at the document,
3 but it is about three inches thick, three or four inches
4 thick.

5 Because there's a methodology is laid out and then
6 they go through, it's sort of like what we've been doing
7 with these chemicals, except looking at different biological
8 parameters and there are a series of studies discussed and
9 distributions involved.

10 But I think it's like the one we just approved,
11 it's going to represent a substantial contribution to
12 improving the quality of these risk assessments.

13 But I think that the plan, since it is
14 complicated, to have it presented at one meeting and give
15 people some time to think about it before we actually
16 discuss it is a good idea.

17 But I have, in going through it so far, I haven't
18 found any major problems, although I'm not finished.

19 DR. MARTY: Okay.

20 CHAIRMAN FROINES: Can I ask you one question
21 before we go on.

22 One of the issues that emerges when you do
23 stochastic modeling and you've looked at the population
24 distribution of risk, that gives you a whole series of data
25 which you then use in your ultimate risk management

1 determinations.

2 Here we come up with 3 times 10 to minus 4 for
3 diesel, and then unfortunately, in my view, people tend to
4 use that as a bright line.

5 Now, with stochastic modeling, you come up with a
6 wide range of values, based on the different distributions,
7 and then somebody has to decide what is the level of
8 protection that you should afford the public, given those
9 distributions.

10 And so it would be very useful when we actually
11 get around to discussing it, I don't want -- the panel can't
12 get into the risk management issue, but if you can give us
13 some sense about how you developed this mass of data, how
14 people are going to interpret it for public health
15 consideration and control use, because if you have 25
16 numbers or ten numbers or one number or hundred numbers,
17 somebody still has to decide what is the -- what do you use
18 when you make decisions.

19 And so at some level just because you can do
20 stochastic modeling doesn't mean that things get necessarily
21 better, unless you have a clear, coherent policy framework
22 to offer. So it seems to me it would be useful to have some
23 sense for the panel to have some sense of that, so they have
24 a sense of how you're actually going to use that
25 information.

1 DR. GLANTZ: I'll let Melanie talk here, since she
2 wrote the document, but that's in there actually. You know,
3 where they in fact have some discussion of when it's worth
4 the trouble or suggestions on how to decide whether or not
5 it's worth the trouble to use this more complicated modeling
6 approach. I don't recall anything about where you should
7 draw the line.

8 DR. MARTY: Right. We actually presented tiered
9 approach in there to risk assessment, with four tiers. The
10 first being just a deterministic approach where you have one
11 input value for an exposure parameter, and that would be the
12 simplest form.

13 And what we did was we used our analyses of the
14 distributional characteristics of the data, for example, for
15 breathing rate, to say where we think those point estimates
16 should lie and we present a mean or a central tendency
17 estimate and a high end estimate, which in this case is the
18 95th percentile on the distribution.

19 And then we do have discussions of when it makes
20 sense or doesn't make sense to do a more complicated risk
21 assessment using the full distribution.

22 We do -- we don't have anything in there about how
23 the risk manager then chooses where on the distribution
24 they're going to protect people. And we did that in a sense
25 on purpose because we're trying to just look at the science

1 and say this is the 50th percentile, this is the 75th, this
2 is the 90th, this is the 95th, rather than getting into the
3 risk management end of things.

4 However, both the Air Board and several of the
5 districts have had some discussion about this issue and I
6 anticipate a lot more discussion in the next six months or
7 so of what to do with the numbers.

8 In essence to have the distributional
9 characteristics better defined helps the risk managers,
10 because right now the deterministic methodology is based on
11 estimates that might be a combination of the 50th percentile
12 and the 75th and the 95th here and maybe the 99th there and
13 you really don't know where you are on the distribution
14 without doing a really thorough analysis. So that's one of
15 the issues that we tried to address in this document.

16 CHAIRMAN FROINES: Go ahead.

17 DR. MARTY: Okay. And then Parts 1 through 4
18 represent the technical support documents, with lots of
19 information that eventually gets distilled into Part 5,
20 which is risk assessment guidance manual. The guidance
21 manual is just that, it's a step-by-step incorporates all
22 the information from Parts 1 through 4 and gives
23 instructions for conducting site-specific health risk
24 assessments in the Air Toxics Hot Spots Program.

25 And we have worked with ARB on this and will

1 continue to do so and also with the California Air Pollution
2 Control Officers' Association.

3 We're hoping that the manual is ready by this
4 summer.

5 There was some discussion about the role of the
6 panel, but we think that the panel needs to look at the
7 manual.

8 That's all the overheads that I had.

9 DR. GLANTZ: That's all the work you have for us?

10 CHAIRMAN FROINES: So panel will see the manual
11 this summer?

12 DR. MARTY: Yes.

13 DR. COLLINS: Jim Collins, OEHHA.

14 I'd like to say that some of the acute RELs are
15 already being used now in risk assessments that the
16 districts are submitting to OEHHA, so the numbers that were
17 approved last March have been actually used in actual risk
18 assessments or as an index or acute index.

19 CHAIRMAN FROINES: So, Melanie, you were going to
20 say?

21 DR. MARTY: There were some concerns on a couple
22 of the panel members regarding the use of the chronic
23 reference exposure levels. And I don't have overheads for
24 this, but I think I wanted to talk through it.

25 In particular, since some of these chronic

1 reference exposure levels are fairly close to measured
2 ambient concentrations in the South Coast Air Basin, the
3 question arose, well, what does the risk manager do with
4 that.

5 The hazard index approach, as you'll recall, is
6 where you ratio the modeled ground level concentration from
7 what you estimate using modeling the air dispersion of
8 chemicals from a specific site. You ratio that to the
9 reference exposure level.

10 If that number is one or less, then the typical
11 risk management decision has been that the facility is fine
12 and it poses no public health risk.

13 It's when this number goes above one that flags
14 get raised. Different risk management, just different risk
15 managers will use that number in different ways. The 35 air
16 pollution control districts all have to have a regulation as
17 to what they do for the hot spots program when that number
18 goes above one.

19 In the notification provisions of the statute, the
20 district can require facilities to notify the surrounding
21 community of their emissions and what those emissions are,
22 what the potential health impacts are.

23 It's up to the district whether they notify and
24 who notifies.

25 The ARB back in '92, I think, came up with a

1 notification guidance, and in the guidance they recommend
2 that OEHHA be contacted if the hazard index goes above one.
3 And there was a lot of discussion and still is a lot of
4 discussion about what to do when the hazard index goes above
5 one. And the primary issue is, well, there's uncertainty in
6 those numbers. Those numbers are meant to protect basically
7 everybody, so when you start exceeding those numbers, how
8 much do you have to exceed them before you actually have
9 endangerment of the public health.

10 Of course we have included information in there to
11 protect sensitive subpopulations.

12 So there have been many instances where the
13 districts have a facility where a hazard index is above one
14 and they've called us and said what is the uncertainty in
15 this number and we've walked them through the derivation of
16 the reference exposure level.

17 If we have an uncertainty factor of a thousand and
18 the hazard index is two, that doesn't give me very much
19 heartburn and generally doesn't give the risk managers very
20 much heartburn.

21 If you have a hazard index of two or three or four
22 and your uncertainty factor was only cumulative uncertainty
23 factor of ten, then in most instances most districts would
24 require that facility to notify.

25 So it's not hard and fast. Some districts have --

1 at least one district, Sacramento Air Quality Management
2 District, the hazard index has to reach ten before they
3 require notification.

4 I don't personally necessarily agree with that,
5 because that erases all of the uncertainty factor for some
6 chemicals, but for others that may be adequate. So therein
7 lies the rub of how to use these numbers.

8 DR. FUCALORO: So the reporting of a number, of
9 course, is one-dimensional object element. Why not report
10 numbers with uncertainty factors?

11 DR. GLANTZ: They are.

12 DR. FUCALORO: They do that? So they say contact
13 you and ask you what the uncertainty factor is. It seems to
14 me they should have the information --

15 DR. GLANTZ: It's in the documents.

16 DR. MARTY: They have the documents. They have
17 the documents. It's just usually a question, it's an
18 engineer who is calling and they're unsure of the meaning
19 and the toxicology of the compound and want to know a little
20 more. That's generally what happens.

21 DR. FUCALORO: Also I mean an argument for a
22 case-by-case basis, not only knowing a number and an
23 uncertainty factor, also the toxic endpoint is important.

24 DR. MARTY: Yes.

25 DR. FUCALORO: If it's sneezing, it's one thing.

1 If it's something neurological damage, it's quite another.

2 DR. MARTY: Yes, yes. I think most risk managers
3 get a little more nervous if we're talking about
4 developmental toxicity and irreversible impacts, versus eye
5 irritation.

6 CHAIRMAN FROINES: But there's also the issue of
7 variability versus uncertainty.

8 DR. FUCALORO: That's a good point. That's a good
9 point.

10 DR. MARTY: Yes.

11 DR. GLANTZ: And the stochastic model or document
12 goes on in some length about that, actually.

13 CHAIRMAN FROINES: So is there -- do the local
14 districts -- let's assume if the local districts then have
15 the company or whoever notify the public who are quote,
16 "overexposure," is there any other legal requirement for
17 control to reduce that level?

18 DR. MARTY: Yes. There is a requirement that the
19 districts, if they deem the health risk to be significant
20 enough, institute risk reduction audits and plans, so the
21 facility has to go back and look at their process and decide
22 where they can reduce emissions.

23 To my knowledge, there have been very very few
24 facilities in this state that have had to do risk reduction
25 audits and plans, and it's always been based on the

1 carcinogenicity, or the carcinogenic risk from the
2 emissions. I'm unaware of any risk reduction plans that
3 have been triggered by a hazard index exceeding one.

4 DR. COLLINS: They could be.

5 DR. MARTY: Yes, they could be, but I'm unaware
6 that that has happen.

7 I think in most cases they have a different
8 trigger level, so, for example, the notification, the
9 trigger level might be a hazard index of two or five, but
10 the risk reduction trigger level is much greater than that.
11 They've done that also with the cancer risk estimates from
12 facilities. Most facilities have to notify when the cancer
13 risk is above ten to the minus five, but risk reduction
14 doesn't kick in until the cancer risk is above ten to the
15 minus four. There's a parallel. Each district has their
16 own regulation, so I don't know what all the regulations
17 are, but there's a parallel process for the hazard index.

18 DR. COLLINS: The South Coast is currently looking
19 at revising the hazard index, get your hazard index below
20 five, and now they're thinking of getting it below three, so
21 that's part of the rule 1402 that we're looking at right
22 now.

23 CHAIRMAN FROINES: Well, it's interesting --
24 Peter.

25 DR. WITSCHI: These are great documents. Are they

1 are going to be available in some electronic form?

2 DR. MARTY: Yes. They'll be posted on our Web
3 page, so people can just download them from the Web page,
4 from OEHHA's web page.

5 DR. WITSCHI: Are they going to be searchable in
6 these form?

7 DR. MARTY: Are they going to be circulated?

8 DR. WITSCHI: Searchable.

9 DR. MARTY: Searchable.

10 DR. WITSCHI: The reason I'm bringing this up, I
11 once came across documentation which was on a disk, but it
12 was in pictures. It was totally useless, because you
13 couldn't search it.

14 DR. MARTY: You know, I have to ask our Web
15 master.

16 Andy says there is a search tool on our Web site,
17 but I personally never tried it, so I don't know how good it
18 is.

19 DR. SALMON: It's a basic text search function at
20 the moment. I think they're looking into getting more
21 sophisticated database type structure built into the site,
22 but it's not there at the moment.

23 DR. WITSCHI: Because the data you have in those
24 documents, they really could be used to do some very
25 interesting research and reexamination, re-evaluation of

1 some of the assumptions, because we have so many data on
2 them.

3 DR. SALMON: It's a basic long-term objective to
4 get all these numbers into a database format, so it would be
5 actively searchable off the Web site, and that's something
6 which they're working on at the present time.

7 DR. MARTY: I think there's another issue to sort
8 of tie it in there, what do you do when your reference
9 exposure level is pretty close to ambient measured
10 concentrations. And it's really parallel to if you look at
11 the criteria air pollutants we do have some RELs for the
12 criteria air pollutants, basically they're the ambient air
13 quality standard. And many times they're exceeded in the
14 basin.

15 Some years back, the districts required facilities
16 to also in this program look at their criteria air
17 pollutants emissions and add them into the hazard index
18 approach, and in the South Coast Basin that almost always
19 kicked people over one for respiratory and eye irritation,
20 so the district made the decision not to require people to
21 notify based on a criteria air pollutant emission if that
22 exceeded that, the ambient air quality standard.

23 And part of their logic was, well, we have other
24 ways of dealing with that, we don't need to deal with that
25 through the Air Toxics Hot Spots Program. There's a whole

1 nother program that deals with criteria air pollutants.

2 So in the case of formaldehyde there may be for
3 this chronic REL, it's fairly close. It's actually the
4 ambient levels measured in '98 are right on top of what
5 we're proposing as the chronic reference exposure level.

6 So it may turn into an issue for the risk manager
7 of whether they want to do something about that or not.

8 CHAIRMAN FROINES: I have just one more question,
9 which is let's assume that you have a plant that's using
10 toluene diisocyanate, which is a strong sensitizer, that the
11 effects are very low levels and so on and so forth.

12 How does anybody know that plant X, which used the
13 TDI, and how does anyone know what that dispersion
14 concentration is? In other words, how does one determine
15 the numerator in your hazard index, and how is -- are the
16 local districts responsible for determining that those
17 values for industrial sites and so they have to know what
18 chemicals are being used? I don't understand how it all
19 works, frankly.

20 DR. MARTY: The districts are required to obtain
21 information on emissions from the facilities themselves that
22 are under their purview. And there are cut points in terms
23 of if the facility emits greater than 25 tons per year of
24 criteria air pollutants than they were in the first phase.
25 And there's the first phase, the second phase and the third

1 phase, basically go by size of the facility.

2 The districts generally have gone by which
3 facilities have permits. So that's how they've tracked
4 facilities down. They work with the facility operator to
5 come up with the emission estimate, and they're responsible
6 for making sure that the emissions estimates from each
7 facility are accurate.

8 For a small district that's a small workload. For
9 the South Coast Air District that's been a huge workload.

10 If the facility is required to conduct a risk
11 assessment, and only those that fall within a certain
12 category in the district's prioritization are actually
13 required to write a risk assessment, for those facilities
14 the risk assessment uses an air dispersion model to estimate
15 what the ambient concentrations are in a grid surrounding
16 the facility. That air dispersion model is reviewed by the
17 local air district engineers and approved.

18 So and also the Air Resources Board is sometimes
19 called in for some of the more -- the larger facilities that
20 had to use fancier modeling.

21 So that's how the numerator is derived. It's
22 basically based on estimates of emissions and air dispersion
23 modeling.

24 CHAIRMAN FROINES: Further questions? Are there
25 further questions for Melanie?

1 Okay. Thank you.

2 Can we take a ten-minute break before we switch
3 over to pesticides.

4 (Thereupon a short recess was taken.)

5 CHAIRMAN FROINES: Everybody has a copy of the
6 January 5th letter to Paul Helliher and Mike Kenny that
7 transmitted the findings from our two -- our workshop that
8 had two parts, one on prioritization and one on exposure
9 estimation. And so you've had that before, so this is just
10 give it to you again.

11 It seems to me that that process worked out very
12 very well.

13 So the point of this part of the agenda is for a
14 discussion to see if the panel has ideas for any subsequent
15 workshop activities that we might consider to further
16 improve our addressing of pesticide-related issues.

17 And I think that the other part of this would be
18 for Elinor to work with DPR staff to further develop ideas
19 and generate suggestions.

20 And I think what she's going to mention this
21 morning is not a direct result of a conversation with DPR,
22 but in a sense her own activities. But that one of the
23 things we did was to ask Elinor to work with staff at DPR to
24 develop workshop ideas so that we're all in sync on this.

25 She has some suggested ideas for future workshops,

1 the dates of which are to be determined.

2 And basically she thought that we never completely
3 finished the issues surrounding organophosphates.

4 So, Elinor, why don't you talk about the things
5 you've been thinking about?

6 DR. FANNING: Do you want to start directly with
7 the organophosphate idea, or do you want to open for a more
8 general discussion of more a brainstorming for future
9 workshop topics? We can do it either way.

10 CHAIRMAN FROINES: Either way. Go ahead.

11 DR. FANNING: Okay. I had via Jim Behrmann for
12 input before today's meeting from either panel members or
13 agency staff for ideas for future workshops.

14 I think perhaps the time was a bit short, and I
15 haven't heard a lot of feedback yet.

16 But we can have a general brainstorming session
17 today in which we can identify topics that might be helpful
18 to discuss in a workshop format. And I think the idea is if
19 we can anticipate the issues, scientific issues, that are
20 likely to arise in the evaluation of documents that are
21 coming to the panel, then I can work to develop an agenda
22 and identify some speakers who can address those topics and
23 get to some consensus and clarification before we actually
24 get into long snarls with various documents.

25 Maybe it is most effective if we begin with the

1 one idea that I came up with, and then we can take a minute
2 afterward to develop this idea further and also see if there
3 are other topics that people would like to suggest.

4 So this is the one-page outline that Peter should
5 have, I believe, handed out to everybody.

6 Okay. What this is is essentially an idea to take
7 a short session, probably just a couple of hours, to follow
8 up on some of the recommendations that came out of our
9 earlier workshops held in October in South San Francisco.

10 Specifically from workshop Part A on pesticide
11 prioritization from October, the second recommendation from
12 the panel is to consider a batched approach for listing of
13 high priority or organophosphate pesticides.

14 And the idea there is to see if DPR would consider
15 developing a document similar to what you're seeing for
16 chronic RELs that would essentially address a number of the
17 organophosphate pesticides in one document and thereby
18 streamline the process of evaluation. Many of these
19 pesticides have similar toxicological properties.

20 So I would envision -- this is just sort of
21 brainstorming of my own, and I think it would be good after
22 I go through it to see if DPR might have some comment on
23 what they think would be most useful out of this.

24 But I envisioned beginning with DPR staff coming
25 with a status report on the organophosphates, going through

1 which ones are their highest priority for assessment at this
2 point, which have been monitored in California. And I
3 believe the majority of the high-priority organophosphates,
4 there is some monitoring data available.

5 Furthermore, there are toxicological and health
6 effect assessments from US EPA, and we had a speaker come to
7 our workshop to discuss those tolerance reassessment
8 documents with us. So there are quite a bit of background
9 data that may or may not be useful for the DPR assessment,
10 and I'd have to get DPR to comment on that.

11 And after we began with an identification of which
12 organophosphates might be useful to address in a batch, then
13 I envision that we could go on and discuss some of the key
14 toxicological issues with assessments to these pesticides,
15 perhaps bringing in outside speakers if that is useful.

16 And the toxicological issues that came to my mind
17 right off the bat, first are the issue that we've had
18 several times before of cholinesterase inhibition. It's not
19 clear to me whether it's completely resolved, how the panel
20 and DPR want to handle evaluation of cholinesterase
21 inhibition data, and whether it might be useful to develop a
22 discussion to develop a standardized approach to those data.
23 Most of these pesticides are cholinesterase inhibitors. So
24 that would be the first of those issues.

25 We can talk about that a little bit more, what

1 specifically you'd like to see addressed, and then I can
2 work to try to identify appropriate speakers for it.

3 Secondly, I identified metabolism and
4 toxicokinetics as an area that might benefit from some
5 workshop type discussion before preparation of a document.
6 There's quite a bit of information on paraoxonases, enzyme
7 in humans and interindividual variability due to
8 polymorphisms in the gene for this enzyme, that may affect
9 the population distribution of sensitivity to
10 organophosphate pesticides.

11 So I had identified that as a potential area to
12 bring in a speaker and have some discussion.

13 And the third toxicological issue that I have on
14 this relates to a discussion that I believe has also come up
15 with the panel before of acute and reversible health effects
16 versus chronic delayed health effects and how those data
17 would be treated in the risk assessment.

18 Item No. 3 would then progress to sort of a
19 discussion of method, what type of format for a batched
20 document would be most useful for the panel and most
21 efficient for DPR to develop some discussion on how to, what
22 type of outline would be most effective.

23 Then the final issue that I thought we may want to
24 include is some discussion of whether or not it's useful to
25 try to address co-exposure to multiple organophosphate

1 pesticides in this document.

2 We had some discussion of multiple pesticide
3 exposure in our workshop. We had the follow-up session at
4 Claremont where Randy Segawa from DPR presented some
5 alternative ways of grouping pesticides. And one of his
6 alternatives was in chemical family types such as
7 organophosphates.

8 So we may want to develop that idea a bit further,
9 but I believe it would require quite a bit of discussion
10 about how to do an exposure assessment for mixed pesticides.
11 We need to look into the feasibility issues there.

12 So that's a brief presentation of the idea that I
13 had for that workshop.

14 And I'd be interested in hearing feedback whether
15 people think it's useful, whether there are issues you
16 particularly like to see. And I don't know if perhaps DPR
17 might want to comment.

18 MR. GOSSELIN: Thank you, Elinor.

19 I thought this was a real good outline. It's
20 consistent with the findings from the workshop from last
21 fall and some of discussions we had. And I think even
22 thinking about the discussion you just had with the OEHHA
23 documents and how they've gone through a pretty lengthy
24 process and batching of many many compounds for
25 consideration, and given the parameters of what the law

1 allows us to do and what would meet the scientific
2 expectations of 1807 could we do something similar. Because
3 I think as a finding, grinding out single documents is kind
4 of a long process. And if there's a more efficient means
5 while maintaining a full scientific scrutiny of the
6 pesticides we're dealing with, we should probably look into
7 that, and I think this might be a good opportunity to do
8 that, looking at the OPs.

9 Another cut on this is that we also have a list of
10 HAPs listed toxic contaminants. Those are out there, some
11 of which we do have risk assessments completed on, some of
12 which because of their use or potential to get into air or
13 other things that we don't have any activity on, but
14 eventually we may have some air issues with them and should
15 there be a means of us going through a similar process you
16 went through with OEHHA of coming up with a summary document
17 and getting RELs established for those compounds.

18 And almost as a sideline is this project we're
19 working on with ARB, OEHHA and some other agencies down in
20 Lompoc, that's going to expand this spring, we're going out
21 and monitoring for upwards of 50 pesticides in a community.

22 CHAIRMAN FROINES: 15?

23 MR. GOSSELIN: 50.

24 CHAIRMAN FROINES: 5-0 or 1-5?

25 MR. GOSSELIN: 5-0.

1 The staffs from OEHHA, our staff and DHS and the
2 county have gone through and using best professional
3 judgment have come up with sort of preliminary RELs that
4 would be used as screening levels for these numbers.

5 So this is almost getting into sort of the cutting
6 edge where pesticide air exposures are getting to the
7 communities, looking at multi-residues.

8 The big advent is going to be that there's going
9 to be multi-residues screens developed for air monitoring
10 that's going to allow us potentially to use these methods in
11 various places, which is going to necessitate having some
12 scientific notice to evaluate whether we need to take any
13 mitigation measures.

14 But I think with this, whatever choice we make on
15 going with OPs, which is a good one, or HAPs, or some other
16 cut, I think looking at the document you've just gone
17 through and approved is almost a template for us to try to
18 emulate, would be a suggestion on how to go.

19 CHAIRMAN FROINES: When you say multi-residue
20 screens, are you doing essentially micro-environmental
21 monitoring to look at contamination of soil, contamination
22 of water?

23 MR. GOSSELIN: The one down in Lompoc is strictly
24 air.

25 CHAIRMAN FROINES: Air.

1 It's an interesting issue when you think about it.
2 If you've identified 50 pesticides that are used in Lompoc
3 that you can sample for, that gives us some sense of the
4 scope of this problem we're dealing with. It would be
5 interesting to see a protocol for what this is.

6 MR. GOSSELIN: Actually, one of the things we're
7 interested in with this project and the protocol is having,
8 and this was just discussed at the interagency panel, was
9 having some external peer review of the work that staff had
10 been doing, so that's real critical. And if that can be
11 brought forward here to evaluate, at least the methodology
12 on how the monitoring is designed and the thought process
13 and screening levels, I think that would be real helpful.

14 CHAIRMAN FROINES: On the HAPs, you know what
15 would be useful, it seems to me, would be to have Elinor
16 work with your staff to look at the use patterns for the
17 various HAPs, as well as the chemical structures for the
18 HAPs. In other words, are there unifying elements that
19 would help pick -- we were talking last night about
20 compounds that contain chlorine and bromine, for example, as
21 one structure issue. And but I don't know the pesticide
22 HAPs, so it would be useful to do some background to look at
23 structure activity issues and to look at use patterns.

24 DR. FANNING: Is there a sense of whether it would
25 be -- I think this idea of looking at HAPs or looking at the

1 group of chemicals being monitored at Lompoc is very
2 interesting, and is there a sense of whether we would want
3 to focus on one of those issues first or the organophosphate
4 groups, or which would be most useful?

5 MR. GOSSELIN: There are down in Lompoc it does
6 capture a lot of OPs used in one of the screens.

7 DR. GLANTZ: Why did you pick Lompoc, just for
8 curiosity?

9 MR. GOSSELIN: Given we only have the rest of
10 today, I don't have all the time.

11 DR. GLANTZ: Can you give us, you know, the
12 classic comic book explanation of why you picked Lompoc?

13 MR. GOSSELIN: They picked us. It was a community
14 that had housing right next to agriculture in the Valley,
15 and fairly small community, moderate size, fairly moderate
16 size agriculture in an enclosed valley, right next to
17 Vandenburg Air Force Base.

18 There was a lot of concern about various health
19 concerns in the community and one of the concerns was some
20 pesticide use. And one of the things that had not been done
21 was very extensive or any pesticide monitoring of
22 agriculture in that area.

23 So it became chicken and egg about which products
24 about the 140 that are used there, what to monitor for and
25 whether they had any direct bearing on the health effects.

1 And that sort of discussion went on for a while
2 and then about three or more years ago we ended up forming
3 an interagency work group with state scientists and brought
4 in some local people to kind of craft out a consensus on
5 what they would like to see.

6 That did go beyond pesticides. There was a silica
7 plant that eventually shut down and they were having a lot
8 of problems and a variety of other things.

9 And there's a big health survey going on also.

10 CHAIRMAN FROINES: But my sense is that we can
11 follow that operation going on there, but it seems like that
12 wouldn't be part of something we would do as a workshop
13 unless -- it seems to me like the outline that you came up
14 with for this makes more sense, at least from our
15 standpoint.

16 MR. GOSSELIN: The cholinesterase policy probably
17 be something very relevant and specific, that we've had sort
18 of our paper written on. I think EPA has held at least one
19 scientific advisory panel on that, with issue papers. I'm
20 not sure if they have a report out yet.

21 DR. FANNING: They do have some kind of risk
22 assessment approach to cholinesterase data.

23 MR. GOSSELIN: Right.

24 And some of the members that sat on the SAP could
25 come out for that also.

1 DR. BYUS: I really like this outline for the
2 organophosphate. Lot of these issues we dealt with and are
3 very important. It's still not clear that -- I really think
4 it would be an excellent idea to have a workshop on this, on
5 the organophosphates. I don't know what the order would be,
6 but it's certainly a pressing issue. There's many of them.
7 And all of these issues, toxic mechanism, toxicokinetics,
8 plasma versus red blood cell, versus brain, delayed
9 neurotoxicity versus immediate, and also the carcinogenicity
10 of these things is complicated. It's variable.

11 And then the multiple exposure issue, God only
12 knows. I mean, I think I still say somewhere in food
13 residue is some answer to that question, because at least
14 you know that these were all applied at one point. If you
15 work your way back from that, in addition from forward from
16 how you've sprayed them, you can work your way backwards,
17 because you know they're actually there.

18 So all of these things are very important and
19 since there's a lot of organophosphates, I think just the
20 science discussion would be very important to the panel.

21 DR. FANNING: Okay.

22 CHAIRMAN FROINES: I frankly think this issue, the
23 more I read about pesticides, the more impressed I am with
24 the tremendous challenge that we have, because the data we
25 have to work with is so limited. We're constantly trying to

1 ask questions and there's no data because people do science
2 for regulatory purposes rather than science for NIH.

3 And so you just don't have the kind of -- I mean,
4 just look at the database on butadiene or perchlorethylene
5 or asbestos or lead. I mean, it's thousands of papers.

6 And with pesticides, there's just a few papers and
7 they're not in the peer-reviewed literature. Relatively few
8 in the peer-reviewed literature.

9 We can try and look at all these issues, which I
10 think is good, but part of the problem is what we have to
11 work with is so small. I wish there was a way to stimulate
12 more research on a lot of these issues, because I think we
13 have a real limiting factor.

14 But having said this, I think there's a third
15 issue that is a little different from what Elinor said,
16 which is I take the issue of chronic health effects from OPs
17 as being different than acute effects as being different
18 than delayed neurotoxicity, and that is the long-term
19 chronic neurological effects from organophosphates,
20 irrespective of the delayed neuro effects is still an issue
21 that is not well defined, I think. So that's another.

22 DR. FUCALORO: I'm a little unsure as to what
23 we're supposed to be deciding here. This looks like
24 basically, it seems to be some agreement, at least from
25 those who spoke, that the document presented to us would be

1 a good working document for the next workshop, and I guess
2 you come back with some modifications for our review, I
3 guess through you, John.

4 CHAIRMAN FROINES: I think basically Elinor is
5 doing her best at trying to get feedback from this panel and
6 so she's dragging --

7 DR. FUCALORO: Well, it's such a well-thought-out
8 document, it's hard for us to say other than it seems good
9 and we should proceed. But actually you heard some
10 comments.

11 DR. FANNING: Yes, the feedback is useful.

12 In addition, I had hoped to get a sense from Paul,
13 from you, how important this issue was versus other issues
14 that you may have in your minds, other questions, other
15 possible workshop topics that you'd like to address.

16 What I'm hearing, I think, is that most people
17 think this would be a good idea to go ahead with as our next
18 workshop. Is that --

19 DR. KENNEDY: Unquestionably.

20 DR. FANNING: Okay.

21 CHAIRMAN FROINES: I think the other thing is it's
22 important to get a lot of feedback input from DPR, because
23 there are lots of scientific questions that they've been
24 wrestling with for longer than this panel has and the panel
25 becomes a place in which those questions can be aired and so

1 it's maybe it's useful to us then, as well as for panel
2 deliberations.

3 DR. FANNING: Exactly. I anticipate that we'll
4 work together closely and essentially have DPR staff
5 identify and help sort of frame these issues in a more
6 specific way. So we'll plan to work together on that.

7 DR. WITSCHI: You know, you comment about not so
8 much science, this is science, may be true, but there used
9 to be a very extant volume and it was called "Pesticides, a
10 Study in Man." And it was edited by Jake Hayes, who has
11 been dead for about seven, eight years or so. But I think
12 we should make an effort, because to the best of my
13 knowledge somebody is continuing this work, and that is for
14 our purposes the first thing to look for to get information
15 is what are the data out there about toxicities of
16 pesticides as we can derive from man. And I would expect
17 that much of the old information might actually still be
18 valuable.

19 CHAIRMAN FROINES: That's true. There's been a
20 consistent level of research.

21 DR. WITSCHI: Yes, yes.

22 CHAIRMAN FROINES: However --

23 DR. WITSCHI: I don't know, I think somebody has
24 created this, but I'm not quite sure, but this could be
25 found out.

1 CHAIRMAN FROINES: On MITC, the person who is most
2 often quoted is Dr. Alexeeff. He has the most references, I
3 think, of anybody. So we expect to hear from you today.

4 Thank you, Paul.

5 Thank you, Elinor.

6 I think we're finished on that.

7 DR. FANNING: Yeah. I think so. We'll work
8 together and send something around with a more detailed
9 proposal after we have worked it out and propose a date and
10 see if you have input about speakers or want to help refine
11 the agenda.

12 CHAIRMAN FROINES: I think that I'm interested in
13 paraoxonase polymorphisms, but I think that you should try
14 and keep the context clear, which is how does the
15 paraoxonase polymorphism or other interindividual
16 variability issues affect the risk assessment process. So
17 it's not just simply an abstract scientific issue.

18 DR. FANNING: Sure. I think as I stated here, the
19 idea is can the data on paraoxonase polymorphisms be used to
20 perhaps adjust or at least provide a reality check on the
21 use of default tenfold interindividual variable protection
22 factor. Perhaps that would help bracket it a bit. One of
23 the goals of discussing it is that very concrete risk
24 assessment issue.

25 CHAIRMAN FROINES: One of the things we might hope

1 to come out of some of these things is questions that we can
2 send to US EPA to say we need to know how many people in the
3 population have this genetic change, and EPA should be
4 funding work to find that out. I mean, in other words, it's
5 not -- we don't necessarily have to see this as a totally
6 internal process, because if we raise important scientific
7 questions, then in fact those should go to a place like EPA
8 for them to think about it. California tends to be ahead on
9 this stuff to some extent, rather than behind.

10 DR. FANNING: Thank you.

11 CHAIRMAN FROINES: Peter and I, we're talking
12 because we were -- Paul Blanc is doing his -- is on the
13 wards at this point, so he can only be here for an hour or
14 two, because he's actually seeing patients. And he played a
15 fairly strong role in the last meeting on MITC, so we were
16 hoping to have him here, but I don't think he can be here
17 until 12:30 or 1:00, so I think what we should probably do
18 is start with MITC, take a lunch break and then finish up.
19 So we don't sort of delay everything just to get one person
20 to the meeting.

21 So, Paul, let's do MITC.

22 MR. GOSSELIN: Staff are getting ready to come up.

23 And, thanks.

24 This is continuation of the discussion on the MITC
25 document.

1 What we had planned on doing, instead of going
2 back over the entire document, is do a couple things.

3 One, just summarize the relevant issues for the
4 toxic side in the document and also kind of focus on the
5 issues. I think Elinor summarized some key issues that were
6 raised from the last meeting and a couple of the other ones
7 that have been raised since that time, and also talk about
8 sort of the status of where we are on looking at what
9 exposures are occurring out there from the data we have had
10 and data we got in December.

11 And also I think Tom is going to look at
12 adjustments to, possible adjustments, to some of the
13 longer-term exposures based upon new use data.

14 A couple things on the importance of this document
15 are twofold, beyond just the consideration of listing MITC
16 as a toxic air contaminant. Your review's also going to be
17 used by us as our external peer review to help support
18 formal rulemaking that may need to occur based upon the
19 issues, the scientific issues raised in this document. So
20 the full review and the consideration of these issues are
21 real critical, not only for the listing process, but also
22 for our regulatory process.

23 With that, and I know there's a lot of issues,
24 I'll turn it over to Andy Rubin.

25 CHAIRMAN FROINES: Just one comment.

1 Remember at the last meeting in November in
2 Claremont, we only got about halfway through, so we haven't
3 really dealt with the risk characterization and risk
4 assessment issue and I think we did some work on exposure,
5 but not enough, I think.

6 And why don't I stop there.

7 But the issue of clearly you've seen what Elinor
8 has raised, but one of the major issues that we need to
9 decide upon is what goes into our -- what goes into our
10 findings, which will then go to Paul Helliher, and in that
11 regard this becomes -- I just want to say this for the
12 panel, because this is an extremely complicated chemical.

13 We have metam-sodium, which has its own
14 toxicologic properties. We have MITC, which has its own
15 toxicologic properties. We have methyl isocyanate, which
16 has very significant toxicologic properties, as everybody
17 knows, because of Bhopal. We have carbon disulfide, and we
18 have hydrogen sulfide, just to list the ones I can think of
19 off the top of my head. Plus I have no doubt that there are
20 others. This is a very reactive compound, series of
21 compounds.

22 So that we're really dealing with a quite complex
23 series of compounds and their breakdown products, and so the
24 panel is going to have to address that particular issue when
25 we send our findings forward.

1 This is not -- we're not dealing with a chemical
2 here. We're dealing with at least five. And so it's
3 important for us to think about that as we think about how
4 we transmit this, whatever we intend to transmit.

5 DR. RUBIN: My name is Andy Rubin, and I'm going
6 to be reviewing the health aspects of the MITC document.

7 In view of the fact, as Dr. Froines mentioned, we
8 did start the discussion of the toxicity of MITC at the last
9 meeting on November 17th, and I gave a fairly complete
10 summary of MITC's toxicity profile, I thought what I would
11 do today was instead of spending a whole hour discussing it,
12 the toxic profile again, I would quickly recap what we
13 discussed there to get us all on the same ground, because I
14 know at least one or two members of the panel weren't there.

15 And then probably the most important slide that
16 I'll show you is to introduce you to some of these
17 difficult, what I call discussion decision points with this
18 chemical, some of which have already been mentioned now by
19 Dr. Froines.

20 Then I'm going to take up probably -- well, the
21 issue that we were discussing back on November 17th when we
22 had to stop, and an issue that Dr. Witschi has encouraged me
23 to look at in a little more detail, and that is whether MITC
24 itself could possibly be considered an oncogen, and I'm
25 going to take a detailed look at that, at that particular

1 study.

2 Then we'll go through the margin of exposure
3 calculations, the reference exposure calculations, hopefully
4 we can do that fairly quickly.

5 And then mention some of the toxicity of some of
6 the other metam breakdown products, in particular methyl
7 isocyanate, MIC, and hydrogen sulfide.

8 And then wrap it up. Okay.

9 By way of recap, if you remember, MITC reached the
10 public consciousness back in 1991, July, when 19.5 thousand
11 gallons of 32.7 percent metam-sodium were spilled in the
12 Sacramento River, causing a release of gaseous MITC and
13 exposure of many people in the local area, particularly
14 around Dunsmuir, to irritating concentrations of MITC.

15 The conclusions of the several papers that came
16 out of the epidemiology on that spill were that despite the
17 fact there were no good measurements for two or three days
18 after the spill, the estimated levels of MITC in the
19 Dunsmuir area, the high estimates, ranged between 140 and
20 1600 ppb.

21 These levels, whatever they are, sent 705 people
22 to the hospital complaining of eye irritation, nausea,
23 throat irritation, with one -- with a possible long-term
24 sequela of condition known as RADS, or reactive airway
25 dysfunction syndrome, a kind of chemical asthma.

1 In setting or beginning to set the acute levels,
2 the acute endpoint levels, we looked to a human eye
3 irritation study. This was a study conducted at UC Davis
4 Medical Center, using about 70 individuals.

5 We came up with a NOEL value of 220 ppb, a LOEL
6 value of 800 PPB.

7 Interestingly, this turns out to be right in the
8 level, these two values, right in the area of the estimated
9 values of MITC in the Dunsmuir area after the spill.

10 CHAIRMAN FROINES: Can I ask a question about
11 that?

12 DR. RUBIN: Yeah.

13 CHAIRMAN FROINES: I'd like to come back to the
14 RADS later, but in your document you say the following.
15 Interestingly, complaints of abdominal pain, diarrhea, rash
16 and cough continued after ambient levels had hit below the
17 published reference level of .4 parts per million,
18 recalculated to .5 parts per million in Alexeeff, et al,
19 1994.

20 That report by George, I haven't read, and my
21 question is that would indicate a LOEL of about .5, compared
22 to your NOEL of about 220, which you select. If you take a
23 LOEL of .5, that gets you down to a NOEL of about .05, so
24 there's a fourfold difference between what your document
25 says George says, and he may want to comment on this, and

1 this value that you select.

2 So I couldn't -- the Alexeeff document seems to
3 suggest significant complaints, abdominal pain, diarrhea,
4 rash and cough, at levels of .5 parts per billion.

5 DR. RUBIN: Parts per million.

6 CHAIRMAN FROINES: Yeah. As opposed to your NOEL
7 of 220 parts per billion.

8 So there's obviously in your own document a major
9 discrepancy.

10 DR. ALEXEEFF: George Alexeeff with OEHHA.

11 Actually I would probably agree with Andy Rubin on
12 his assessment of that, because what you said is correct, in
13 terms of .5, .4 parts per billion, and having those effects.
14 However, the exposure occurred over several days. So
15 actually we have a longer exposure than this particular
16 study conducted. Okay.

17 So there is one is the length of the exposure.

18 The other thing is the issue that in the actual
19 incident that occurred, people were possibly exposed to a
20 higher concentration at first and then a lower
21 concentration. So there's that whole exposure, it wasn't
22 .4, .5 over two or three days, it was some higher
23 concentration and then a lower concentration.

24 Then the other thing points again to your previous
25 comment that the issue of are we talking about exposure to

1 MITC or metam-sodium breakdown products. And those are two
2 different questions.

3 And what happened in the Dunsmuir incident was
4 exposure to metam-sodium breakdown products, of which we
5 think MITC is the primary one, but how do those other ones
6 interact. And that's another question there.

7 So this study here is strictly MITC.

8 So I think it is all consistent, but I think it
9 also shows the variability that we have on some of these
10 questions, exposure time, the other things that are in
11 metam-sodium breakdown products and how do they interact.
12 The issue that this particular exposure study was eye
13 irritation only with an eye mask versus whole body exposure.

14 But I think, surprisingly, is actually to me I see
15 this as consistent, as opposed to really a big discrepancy,
16 but it just points out the variability in responses.

17 And also you can look at that issue as well as the
18 variability aspects where we have a population exposure
19 versus, I forget the individuals, the college students that
20 were involved in this study.

21 DR. KENNEDY: You're also looking at physiologic
22 manifestations of possible antecedent injury, which can come
23 after the fact.

24 CHAIRMAN FROINES: Now, I want to, I really do
25 want to emphasize for this panel to be thinking about what

1 are we taking up here. Are we taking up metam-sodium, which
2 is used at 15 million pounds a year in California, or are we
3 taking up MITC, which is not used at all, essentially. So
4 we have zero versus 15 million pounds.

5 And what we send forward to Paul Helliher, I think
6 should reflect the issue, which -- and I'll leave it at
7 that.

8 But, George --

9 DR. GLANTZ: Can I ask a question about that? And
10 that is does MITC come from anything but metam-sodium in any
11 amount? And I remember I think the document addressed that,
12 but I can't remember what it said.

13 DR. RUBIN: There's, to my knowledge, there's one
14 other pesticide that generates MITC upon breakdown and
15 that's dazomet.

16 DR. GLANTZ: That's right. And that's in the
17 document.

18 DR. RUBIN: Yeah. That's in the document.

19 CHAIRMAN FROINES: Very low.

20 DR. RUBIN: Very low compared to the very high
21 levels of metam that are used.

22 MR. GOSSELIN: John, if I can clarify. It's true
23 MITC as an active ingredient is hardly used and is
24 inconsequential across the state. But the risk numbers and
25 this assessment, the way we're going to use it in regulating

1 is to look at the sources of MITC principally from
2 metam-sodium. So this is actually going to be used by us to
3 regulate metam-sodium use, because of the principal effect
4 of its breakdown products, MITC.

5 CHAIRMAN FROINES: We're going to have to come
6 back to that. This is clearly the fundamental issue for
7 this panel to address. There's a high ridicule value of
8 listing a chemical that's not used, and ignoring a chemical
9 with 15 million pounds, and so we'll come back to that.

10 DR. GLANTZ: Just on that point, I mean, given
11 what Paul said, I mean couldn't this issue be, to some
12 extent, resolved by just changing the title of the document
13 to say metam-sodium and the other compound, what was the
14 other one?

15 DR. RUBIN: Dazomet.

16 DR. GLANTZ: Dazomet and MITC.

17 CHAIRMAN FROINES: Well, I think we can -- I would
18 like, my strategy is I would like us to, if we can, to not
19 send the document back for multiple rewrites, so it never --
20 the next time it emerges we'll all be retired. I'd like to
21 try and see, this is an important chemical, a really
22 important chemical. It would be nice to move the document
23 forward, but we have to be sure in our findings and in terms
24 of how we title the document, and all we can do is recommend
25 is that we address this issue.

1 DR. FUCALORO: Well, I'm not sure if we have legal
2 constraints or just a matter of title. I'm not sure about
3 the legal constraints, but it seems to me we're looking at
4 MITC from all sources, whether it's directly applied from
5 metam-sodium or the other one that I can't recall, or in the
6 future some other brand name comes up which produces MITC at
7 a very high concentration. We certainly want this document
8 to cover that, because MITC is toxicological, and so it
9 would, barring legal constraints, you can say MITC from all
10 its sources.

11 Is that fair enough? I don't know.

12 CHAIRMAN FROINES: Well, no, that's not quite
13 right.

14 DR. FUCALORO: Okay.

15 CHAIRMAN FROINES: As we go further into, and this
16 is why we should go ahead and not get into this discussion
17 right now, because the toxicity of MIC is so profound --

18 DR. FUCALORO: That's where really it really comes
19 from, yeah.

20 CHAIRMAN FROINES: We're going to have to deal
21 with that in the context of this too. So MITC breaks down
22 to MIC -- so I'll just -- I still want to follow up George's
23 comment, which I never did.

24 At some level we set a NOEL of 220. It would be
25 nice, however, to see some language in the document that

1 said -- but given that the Nesterova work and given the
2 Alexeeff work, there could be a NOEL that's much lower. I
3 mean, the trouble is we set these NOELs as though they are
4 in stone and in fact there's a huge uncertainty in these
5 values, as we know. They're defined by, as we all know,
6 from reading Kenny Krump's paper, by the dose choices that
7 people make in setting up the experiments.

8 So it's worth thinking about. It seems to me that
9 we think about sometimes putting in ranges of potential
10 NOELs, as well as -- and then perhaps do your calculation on
11 the MOE, looking at some values. In other words, there
12 are -- it doesn't have to be quite so rigid.

13 Go ahead.

14 DR. RUBIN: I might add to that the other aspect
15 that is very determining in NOEL is the endpoint, and when
16 Russell and Rush, who did the study at UC Davis, chose eye
17 irritation using a set of goggles, that they had made
18 essentially the implicit choice not to expose the subjects
19 via the lungs.

20 So we have -- there's a major uncertainty here
21 that perhaps lung effects could occur at lower MITC levels,
22 not even speaking of any other breakdown products.

23 DR. WITSCHI: Just in interest of precision, I do
24 not think that it was eye irritation. I think it was just
25 blinking, which is not the same thing. And if you sell this

1 study as having shown eye irritation, you open yourself up
2 to criticism, because some people question whether increased
3 blinking rate is an adverse health effect.

4 DR. RUBIN: Right. It was increased blink rate,
5 as well as subjective sense of eye irritation. In other
6 words, people were blinking harder and marking a little bit
7 higher on the scale as to how well they felt, how well their
8 eyes felt in relation to a midpoint of how would you feel if
9 you were cutting an onion.

10 DR. WITSCHI: I know. But that's not quite eye
11 irritation as people would look for into these kinds of
12 things.

13 DR. RUBIN: Okay. Moving on to perhaps even more
14 troublesome area, which we discussed in detail last time,
15 the setting of a subchronic inhalation level at one ppm
16 based on effects measured at ten PPM in rats, at 12- to
17 13-week rat inhalation study.

18 Here what we're looking at are systemic effects, a
19 decrease in weight gain, a decrease -- or an increase in
20 water consumption, and decrease in serum protein, that might
21 be argued as fairly marginal. But in the absence of any
22 other data on subchronic or chronic exposures to MITC via
23 the air, we felt that we had to rely on this study and these
24 endpoints.

25 And I covered these in the last meeting.

1 Chronic effects will -- this issue will take more
2 significance when we have the chronic exposure values.
3 There are of course chronic effects of exposure to MITC. We
4 have no inhalation exposure, which is where the primary
5 human exposure is going to come from. There are fairly
6 serious effects in the dog, vomiting, very pronounced
7 toxicity vomiting, salivation, liquid feces, et cetera.

8 But I want to come back to that when we have
9 chronic exposure data.

10 Next slide.

11 This I think will accent what Dr. Froines has
12 said. There are a number of catch points in this risk
13 assessment that we've struggled very hard with, we've made
14 some conditional decisions and we're interested in the view
15 of the panel on these issues.

16 The first, the use of the Russell Rush human eye
17 irritation study, the preferable use of that, over the
18 Nesterova cat study to establish an acute endpoint NOEL.
19 That we discussed last time.

20 Number two, we also discussed last time the use of
21 the rat 12- to 13-week inhalation study to establish the
22 subchronic endpoint NOEL, were the endpoints serious enough
23 to base a NOEL and LOEL determination on.

24 Number three, this issue came up from Dr. Witschi
25 in the last session, is MITC itself an oncogen, and I'm

1 going to present that data today, and how we're looking at
2 that. And I'm actually going -- this is one area where
3 there actually is some change in our thinking from the
4 document that you have in your hands.

5 Number four, this is a big one, metam and MITC
6 have different toxicologic profiles. Metam, unlike MITC, is
7 a pretty frank carcinogen, causes angiosarcomas in male
8 mice, hemangioma sarcomas in male rats. They're related
9 tumors.

10 It is also an embryotoxic and clastogenic, none of
11 which we see in any clear way with MITC.

12 How do we handle this?

13 The way I've handled it up to this point is simply
14 to include the metam risk assessment as an addendum to this
15 document.

16 I've also got a summary of the metam's toxicologic
17 properties in the MITC document.

18 But we're definitely interested in what the panel
19 thinks about this issue.

20 Then some typical risk assessment conundrums.

21 If we're going to calculate chronic MOEs, do we
22 use a subchronic inhalation study, which we have, or do we
23 use chronic oral data?

24 Number six, use of a tenfold default uncertainty
25 factor to establish the chronic REL for MITC from the

1 subchronic data.

2 It's been argued that perhaps we should be using a
3 threefold uncertainty factor, for instance.

4 And then number seven, the toxicologic
5 implications of other degradation of products.

6 These are the big issues.

7 Okay. The issue of MITC's possible oncogenicity
8 came up in the last session. I had a summary slide at that
9 time that expressed the neoplastic situation in rats that
10 had been exposed, these are CD Sprague-Dawley rats that had
11 been exposed to MITC through the drinking water. I had
12 expressed it at that time in terms of benign and malignant
13 tumors.

14 Upon going -- basically I'm going back to the
15 study and reviewing the study in detail, we decided that
16 it's more helpful to look at the actual histological tumor
17 type, instead of just classifying as the registrants or as
18 the contract lab did, by whether they were supposedly benign
19 or not.

20 This study the rats were exposed to zero, 2, 10 or
21 50 PPM MITC in the drinking water. At the end of two years
22 the survivors were sacrificed. Most of the animals that
23 died, died during the second year.

24 What caught our attention in this study was an
25 apparent rise in multiple benign tumors of the mammary

1 gland.

2 When we went back and looked in detail at the path
3 report, which is quite voluminous on this study, we found
4 that almost all of those multiple benign tumors were
5 fibroadenomas. Fibroadenomas occur in Sprague-Dawley rats
6 at levels as high as 50 percent, and in this study as high
7 as 70 percent. So this is a tumor type that is pretty darn
8 common even in untreated animals.

9 A fibroadenoma is a considered a, quote, "benign,"
10 to use a very non-benign term, a benign tumor by all
11 pathologists. However, it has the capacity to progress
12 either to carcinoma, which would be epithelial in nature, or
13 sarcoma in rare instances.

14 I think most pathologists take fibroadenomas
15 seriously. It has the capability of developing into a
16 malignant cancer.

17 What sort of raised our eyebrows on this study was
18 the incidence rate shown at the very top.

19 Something -- I don't know about operating this.
20 Maybe it's too bright in here.

21 What we see in this study is a 23 percent
22 incidence rate in the controls, rising to 40 percent at 2,
23 44 percent and 47 percent in the dosed animals. A Fisher
24 pair wise comparison at the high dose compared to the
25 control comes out with a P value of .054. This raised our

1 eyebrows.

2 I don't pretend to be a statistician, but when I
3 see a P value that close to .05, it's interesting.

4 What I went therefore and did was classify all the
5 related tumors that I could find.

6 DR. GLANTZ: What's the C-A?

7 DR. RUBIN: That's a Cochran Armitage trend test.

8 DR. GLANTZ: You say greater than .05, was that
9 like that .051?

10 DR. RUBIN: In those tests we come up with Z
11 values and it says come up with a Z value above something,
12 it's greater, it's greater than .05, and I hope I don't have
13 to comment on that any more.

14 DR. GLANTZ: Don't happen to remember what the Z
15 value was?

16 DR. RUBIN: They're incredibility low in all of
17 these.

18 DR. GLANTZ: You mean the Z's are like around
19 zero?

20 DR. RUBIN: Or less than zero. They come out
21 negative.

22 What that points out is that we can't see any
23 obvious dose relation with this effect.

24 DR. GLANTZ: Well, it could be. I mean, you don't
25 want to get carried away with small numbers, although those

1 aren't really small numbers.

2 First of all, .054 is close enough to .05 to
3 bother me, and I do know something about it.

4 But the interpretation that I would put on that
5 would be to say that it looks like you get an effect at very
6 low doses and then it tends to saturate, which may be why
7 you're not seeing a trend effect, but it may be that you've
8 still got -- if you get any of this stuff it tends to be
9 bad, and then maybe there's something in there saturating or
10 something.

11 DR. RUBIN: Yeah.

12 DR. WITSCHI: These are endocrinic-dependent
13 tumors, so your point is well taken.

14 DR. FRIEDMAN: It might helpful to see the actual
15 P value rather than just .05. If it's a .06 we'd feel a lot
16 different about it than if it was .5.

17 DR. RUBIN: I think the way to do it would be to
18 put the Z value on this, but I'll go back and look at that
19 and talk to --

20 DR. GLANTZ: It might be interesting to just pull
21 all of your -- to take zero and everything else and to just
22 pool them.

23 DR. RUBIN: Right.

24 DR. GLANTZ: And, you know, and at that point I
25 bet you would get a pretty significant effect of exposed

1 versus unexposed.

2 CHAIRMAN FROINES: Well, there's a couple of other
3 comments I'll make since you did that.

4 The second date, they clearly have small numbers
5 here. We don't like 20 animals.

6 DR. WITSCHI: Group of 50.

7 CHAIRMAN FROINES: This is surviving. In my
8 laboratory we have a hard time picking up cancers in dead
9 animals, animals that are found dead. So there's that
10 problem. So the numbers are small.

11 The other thing is that the animals clearly didn't
12 like the taste of the water, and so that there's going to be
13 a fair degree of variability, or at least uncertainty, in
14 the amount of water that they actually got in.

15 So when you look at this 40 percent, 44 percent
16 and 47 percent, it's not clear whether the mice, the rats,
17 at 50 parts per million didn't hate the drink taste so much
18 that they weren't drinking as much water and therefore their
19 dose was lower. So there could be some simply dose-related
20 issues at the three dose levels, given the taste of the
21 water.

22 In our arsenic work right now we have to work our
23 tails off to get the animals to drink the water. They don't
24 like the taste of the arsenic. And this is clearly the same
25 kind of phenomenon, so that the trend test, given the

1 circumstances of the study, I think one has to be careful
2 overinterpreting that.

3 DR. RUBIN: Can I respond to that?

4 CHAIRMAN FROINES: Sure.

5 DR. RUBIN: I calculated the statistical values
6 based on the calculated intake of MITC based on the observed
7 water intake. It is very true that any time you put metam
8 or MITC into the water the rats stay away from it. They
9 don't like it. It smells like a rotten egg. However, we do
10 have water consumption values here, so we do have MITC
11 intakes.

12 CHAIRMAN FROINES: Well, I agree. And in the
13 experiments that we're doing currently right now on 400
14 animals and 60 animals per test group, we are collecting
15 water data and the animals knock the water -- they don't
16 like the water, so they knock the bottle, they do all sorts
17 of things.

18 So when you actually do this for a living, you
19 have to have some humility about these water intake numbers
20 that you get.

21 DR. FRIEDMAN: I'm confused now, because what
22 you're showing across the top is concentration. It doesn't
23 show the total intakes. So how do we know that that's the
24 total intake?

25 DR. RUBIN: It's in the document.

1 DR. FRIEDMAN: It isn't the concentration, you're
2 looking at the total amount consumed?

3 DR. RUBIN: What we're looking at here is the
4 concentration in water in PPM. We make a calculation and
5 the register -- the contract lab also makes a calculation of
6 the amount of MITC that the animals actually consumed, based
7 on the amount of water that they drank.

8 So those figures are the relevant figures for
9 calculating any statistical values, recognizing that there
10 is a big variation in the amount of water intake even within
11 the same dose group.

12 DR. FRIEDMAN: But it would be helpful to see a
13 table like that based on intake. Do you have those data?

14 DR. RUBIN: I have them, but I don't have a slide
15 on them.

16 DR. FRIEDMAN: Do they show similar finding with
17 sort of the threshold and then leveling off or what?

18 DR. RUBIN: That's what they show. I mean, I'm
19 not sure what you're getting at, but the intakes do vary,
20 I'd say 20-fold. The intakes vary, the mean intakes vary
21 20-fold from the lowest to the highest dose.

22 So it's not terribly skewed to say just present
23 the concentrations, although I would be quite willing to.

24 DR. FRIEDMAN: The intake was fairly similar
25 across those three?

1 DR. RUBIN: Yes. But they're big big --

2 CHAIRMAN FROINES: Big concentration.

3 DR. RUBIN: Big.

4 CHAIRMAN FROINES: And therefore the data is
5 probably skewed, so some animals are going to be having a
6 much higher dose than others or a much lower dose than
7 others.

8 DR. BYUS: Within a group, you're saying?

9 CHAIRMAN FROINES: Yeah.

10 So all I'm saying is we need to interpret this
11 data with some caution where you have obvious evidence that
12 the animals had difficulty drinking the test chemicals,
13 that's all.

14 DR. FRIEDMAN: Another point is that we're
15 focusing on the multiple tumors on the top line, but the
16 second row shows singles where there seems to be no effect
17 at all. I'm a little bit confused as to how to interpret
18 all this.

19 CHAIRMAN FROINES: Can you say something about
20 that? I don't understand this focus on single tumors. I
21 don't understand the relevance of it.

22 Do you, Peter?

23 DR. WITSCHI: No. You can have one tumor or seven
24 tumors. Look at tumor-bearing animals, not the number of
25 tumors.

1 DR. RUBIN: This is tumor-bearing animals.

2 DR. WITSCHI: What's the difference between the
3 rat that has one tumor or three tumors or four tumors?

4 DR. RUBIN: I made that division because partly
5 because the division is made in the data itself. The way
6 this experiment is done this is quite interesting. The
7 pathologist comes along and he sees a big lump in the
8 animal. These fibroadenomas are huge. And while there's
9 one lump, there's a single adenoma. If there are two, it's
10 multiple.

11 The reason I expressed it here was I thought that
12 it might provide -- the reason I went to look at it was that
13 I thought that single fibroadenomas if they were being
14 stimulated by MITC would also show an increase.

15 Perhaps it's irrelevant.

16 CHAIRMAN FROINES: I would draw the conclusion,
17 I'd say the more potent, the greater the dose, the more
18 tumors you're likely to see.

19 DR. WITSCHI: You're right. There are certain
20 systems where tumor multiplicity is really an index of
21 carcinogenic potency. And in this case I really do -- I do
22 not see any reason to separate the animals in the single
23 ones.

24 DR. RUBIN: They're all added up.

25 DR. WITSCHI: If you look at the bottom line,

1 that's very close. If you just add up the tumor-bearing
2 animals, first of all, regardless of whether it's benign or
3 malignant, I think that when we in science and judgment in
4 risk assessment there's a statement that you really should
5 not make a difference between benign tumors or malignant
6 tumors in evaluating bioassays, because uncontrolled growth
7 is uncontrolled growth. And that's where I come from. This
8 is for animals.

9 And then if you really look at the bottom line,
10 that was my point, the ones which have been exposed to have
11 more.

12 Now, you also brought in the historical
13 background. But, see, there's one thing we do not know.
14 Does a carcinogenic treatment increase tumors proportional
15 to the number of spontaneous tumors or does it add tumors?

16 In other words, if you had a background of ten and
17 you have 20 tumors or an incidence of 20, does this mean the
18 incidence was doubled or if you would have only the percent
19 incidence you would have 11 percent in the treated ones.
20 You do not know what is the proportion to the background or
21 something that's being added.

22 And again we're looking at this from a frankly
23 from a conservative standpoint.

24 DR. RUBIN: Yeah. Yeah. I'm well aware of that
25 and I've --

1 DR. WITSCHI: Then the other one, this seems to be
2 a tricky compound, because if you look at the
3 hemangiosarcomas in the metam and your rats have exactly the
4 same phenomenon, you have the paradoxical one, you have a dose
5 response and you have a small increase. Knowing the metam,
6 you actually added the mouse study showed a carcinogenic
7 response, therefore you said the data in the rats mean it's
8 a carcinogen, but if you look at table 9 in your metam and
9 compare it with the human data, they're as good or as lousy
10 as they are --

11 DR. RUBIN: Oh, yeah. This is very real-world
12 data.

13 DR. FRIEDMAN: If we take then the tumor-bearing
14 animals as the criterion, the best criterion to use, then
15 the findings there in the third row are not significant.
16 That's bottom line, the multiple plus single.

17 CHAIRMAN FROINES: Which one are you at?

18 DR. RUBIN: In the third row from the top, right?

19 DR. FRIEDMAN: Yes.

20 DR. RUBIN: When you add all animals bearing
21 fibroadenomas, at least fibroadenomas that can be palpated,
22 you don't get a statistically significant response, although
23 you do still get a slightly higher response in the dose
24 downs.

25 DR. FUCALORO: If I understand Hanspeter, you look

1 at the bottom line, which contains not only the benign, but
2 the malignant, and the same conclusions I think
3 statistically at least from my eye, there's not much
4 response.

5 DR. KENNEDY: Has this been done, Hanspeter, in a
6 strain that does not produce spontaneous fibroadenomas?

7 DR. WITSCHI: What?

8 DR. KENNEDY: Has a comparable study been done on
9 a strain of rat that does not have spontaneous
10 fibroadenomas?

11 DR. WITSCHI: I don't think so, no.

12 DR. KENNEDY: Clearly could be a hormonal effect
13 rather than a direct effect. Very interesting to evaluate
14 it. And one can actually make an argument that the vascular
15 tumors are also at least in part hormonally mediated,
16 because it's angiosarcomas of the breast are rare, but not
17 vanishing, where in humans it occasionally will have
18 receptor-specific hormonal --

19 DR. WITSCHI: Your point is very well taken, but
20 then we have to answer that question, we have to go into the
21 mechanisms. They're facing the same situation as we are
22 facing with certain steroid tumors, where we do get more
23 lumps, but it's clearly a non-genotoxic mechanism and it's
24 the MITC only to answer this question.

25 DR. RUBIN: This is the data for MITC right here.

1 DR. WITSCHI: Yes, I know.

2 DR. BYUS: I have one question. There were really
3 50 animals per group, 26 were live at the end?

4 DR. RUBIN: There are 60 animals per group, yeah.

5 DR. BYUS: So why are they all dying? What are
6 they dying of? I mean even in the control, the control is
7 zero, you're saying to me that there are 60 animals in the
8 group and only 26 of them lived to the end of the study?

9 DR. RUBIN: That's right.

10 DR. BYUS: In my opinion that makes this study
11 virtually useless. Why are the animals dying? You don't
12 want more than half your animals dying before the end of the
13 study of something that's not related to the cancer. I
14 mean, it becomes -- it's a worthless study. You shouldn't
15 even be, perhaps I'm exaggerating because I didn't read the
16 study, but the last thing you want is animals dying. The
17 fewer the better, unless they're dying of the cancer, in
18 which case you make -- that pathologist makes that
19 diagnosis.

20 DR. RUBIN: Right.

21 DR. BYUS: If the animals happen to die during the
22 study, you autopsy them immediately and hopefully determine
23 what the cause of death was and hopefully it's because of
24 the cancer that you're looking for and not something else.

25 If it's something else, you try to make a

1 diagnosis if you can.

2 But I mean to have that many animals dying, this
3 skews all the data completely. You can't get any incidence
4 values that are meaningful out of a study where more than
5 half are dying.

6 CHAIRMAN FROINES: Well, the problem is that when
7 they do die, unless you can pick them up right when they
8 die, you know, everything turns liquid in their insides and
9 so you can't really do pathology. You can find big tumors,
10 but you can't do as precise a pathology as you could do if
11 you sacrificed them.

12 So you really lose data with these animals that
13 are dying from virus infections or whatever is causing it.

14 DR. BYUS: It skews the value --

15 CHAIRMAN FROINES: They are down to a point
16 where -- I have talked at great length with the National
17 Institute of Environmental Health Sciences precisely about
18 this issue, because my current mice are in 16 months and
19 they're dying off, and I wanted to figure out how to deal
20 with this issue.

21 They said we will look at the data down to about
22 20 animals, but below that we won't use it.

23 So that these numbers here are really on the
24 border. And so one has to worry about interpretation. So
25 it seems to me that one can say that there are some trends

1 here, but my concern is that the overanalyzed data, like
2 looking at single versus multiple, it doesn't help. It
3 doesn't tell you anything when you're all finished.

4 And I'm speaking not now as a scientific reviewer,
5 but as somebody who actually does this in the lab, as Peter
6 does, and these are issues that are real, not abstract.

7 DR. BYUS: I'm still saying if your mice are dying
8 of viruses or whatever, something not related to the
9 chemical, and they have this high of percentage that are
10 dying, it skews -- the data becomes meaningless. I do the
11 studies too. And if my animals are dying in this high
12 amount I cancel the study and conclude it, end it. You
13 don't know why they're dying.

14 CHAIRMAN FROINES: You must have much more money.

15 DR. BYUS: I have a very good animal facility.

16 DR. FRIEDMAN: In human studies we deal with this
17 all the time.

18 DR. BYUS: But not in animal studies where you're
19 designing an experiment to assess the carcinogen incidence,
20 incidence in a lifetime and you're doing lifetime studies,
21 which are hard to do. The last thing you want are the
22 animals dying of some other cause other than your chemicals.

23 DR. FRIEDMAN: If you do, it would --

24 DR. BYUS: They might have gotten the cancer, they
25 might have not. They died early from a virus that could

1 have gone on to develop a tumor. You really don't know.

2 DR. FRIEDMAN: There are statistical methods for
3 dealing with this when you -- they're censored at the point
4 that they die and you just take into account the time of
5 follow-up. We have in human studies we have life table
6 analysis and so on to deal with that.

7 DR. BYUS: When you are doing large numbers, but
8 small numbers you cannot do it.

9 DR. FRIEDMAN: If you get too small a sample, then
10 you're in trouble, or if you require that they all live to a
11 certain point, then I see that you're in trouble.

12 CHAIRMAN FROINES: Can I ask you --

13 DR. GLANTZ: Actually, though, I'm sitting here
14 doing some arithmetic on all your numbers. But Gary raises
15 an interesting question, why don't you do a life table on
16 these animals, because you can, if they've lived to a
17 certain point and then died from an unrelated cause, that's
18 exactly what a life table analysis is for, is to take
19 advantage of the fact that you've been able to follow them
20 up to some point and --

21 DR. BYUS: The beauty of doing an animal
22 experiment is it's a controlled experiment. You're
23 designing it to get rid of all these variables and if you
24 don't get rid of the variables your experiment isn't valid.

25 DR. GLANTZ: Right. But if the animal dies of a

1 viral infection or some unrelated thing, you can still take
2 advantage of the fact that --

3 DR. BYUS: A small number. Out of a group of 60
4 you probably would not want more than five die from viruses.

5 CHAIRMAN FROINES: No, no.

6 DR. BYUS: That's all I ever had.

7 CHAIRMAN FROINES: No.

8 DR. BYUS: Many lifetime --

9 DR. WITSCHI: I would have to take issue with what
10 you said. In a study like this, you do not necessarily
11 expect the animals to die from your carcinogen, because it
12 makes a difference if the animals dies from the tumor or
13 whether it dies with the tumor. If it dies with the tumor,
14 that's --

15 DR. BYUS: The zero group is not getting any
16 chemicals and two-thirds of the animals are dying. That's
17 not good.

18 DR. WITSCHI: We don't know if they were dying --

19 DR. BYUS: It doesn't matter when they died,
20 they're supposed to live a lifetime of two years.

21 DR. WITSCHI: No, no. This table doesn't tell you
22 whether the ones who died before terminal sacrifice died a
23 couple of weeks or a couple of months before.

24 CHAIRMAN FROINES: Anyway, this is the only study
25 we have.

1 DR. RUBIN: Right.

2 CHAIRMAN FROINES: We don't follow your point of
3 view and throw it out. You have to use it for whatever we
4 can get out of it and the life table analysis is the classic
5 way that one would evaluate data where you have changing
6 mortality.

7 And so that's that. So I don't think we have
8 another choice.

9 And I think that there are a couple of issues that
10 we'll talk about a little bit later. I mean, one should
11 look at this data precisely because we have metam-sodium
12 data.

13 One has to be thinking about the question of is
14 the MITC the carcinogen, since it is a primary breakdown
15 product, how does its carcinogenicity compare to the
16 metam-sodium carcinogenicity and that's a question that
17 requires some analysis.

18 But I don't understand what the decedents are.

19 DR. RUBIN: These are the animals that died, most
20 of which died in the second year.

21 CHAIRMAN FROINES: You're right. I certainly
22 wouldn't include them.

23 DR. RUBIN: No. You can tell, the fibroadenomas
24 are much lower.

25 CHAIRMAN FROINES: Of course they're dying before

1 you want the study is over, so you can't look at them in
2 terms of any kind of trends. You have to be very lucky or
3 have a very powerful carcinogen.

4 DR. WITSCHI: What really we should do is look at
5 compared when they died off with other studies. In very few
6 studies you get your 60 animals to the ripe age of two
7 years. It does make a difference if they died between 18
8 months or 24 months or if they died between six and ten
9 months.

10 DR. RUBIN: Most of the animals died around the
11 90-week level, between 18 and 24 months.

12 I took this, without knowing about this strain in
13 particular, the CD Sprague-Dawley, I took this as the
14 normative life span of these animals and perhaps there was
15 something particularly morbid about their treatment, but I
16 thought it was the normative life span. Many of them were
17 dying around 90 weeks, 95 weeks, 98 weeks.

18 DR. WITSCHI: That's pretty far into the
19 experiment.

20 DR. RUBIN: The experiment is 104 weeks long.

21 DR. FUCALORO: Can I ask a question? Is it indeed
22 a fact that they only deal with different types of rats and
23 you have no controlled experiments on them, but this would
24 imply that in the lifetime of this particular rat 50 percent
25 of them experienced tumors?

1 DR. RUBIN: That's right. Spontaneous
2 fibroadenomas.

3 DR. FUCALORO: And that's not surprising results
4 to people who know --

5 DR. RUBIN: That is not surprising at all. Leslie
6 Folts in his book "Neoplastic Development," mentions the
7 Sprague-Dawley rat in particular, and says 50 percent of
8 Sprague -- as much as 50 percent of Sprague-Dawley rats
9 develop fibroadenomas.

10 It is my personal position, given the way this
11 pathology is done in this experiment, just by taking lumps
12 and then slicing the lump and doing the histology that way,
13 I think that it's quite possible that every animal in this
14 study that survived had fibroadenomas.

15 The ones that are counted, the ones that are
16 counted are the ones that grew big enough to make lumps. If
17 you actually look at the mammary histopathology, you
18 occasionally -- and the way they do it in a study like this
19 is just take some normal mammary gland and do a section,
20 boom. They don't -- these are not step sectioned, they are
21 not quantitative histopathology. And occasionally you see a
22 normal appearing piece of mammary gland showing a
23 fibroadenoma. If you took -- how many mammary glands do
24 rats have, eight or ten or something? If you did
25 quantitative sectioning, my guess is you would see

1 fibroadenomas in every one of them.

2 CHAIRMAN FROINES: Let me make --

3 DR. FRIEDMAN: It's not a very good control group
4 then, because hundred percent are going to get it. What
5 chemical would make a difference --

6 DR. BYUS: If they live along enough.

7 CHAIRMAN FROINES: Here's the thing. You end up
8 with 6 out of 26 and can you combine multiple fibroadenomas
9 and carcinomas, you get 6 out of 26, 9 out of 20, 16 out of
10 32, and 15 out of 32, and clearly there's going to be some
11 statistical significance at those higher values.

12 Now, everybody agrees this is a lousy study. I
13 think no matter what your point of view we can all agree to
14 that, this was not as well conducted as one would like.

15 But we have to be careful to reward the industry
16 for doing a lousy study. I mean if somebody is going to do
17 a poor study and they have a vested interest, one, it
18 doesn't necessarily test their integrity, but one has to say
19 we don't want to reward that poor study.

20 So it seems to me that you have to take the data
21 at some level on its face value, and say we don't know
22 whether there is a problem, but there could be.

23 It seems to me that it's clearly not black and
24 white. It's clearly gray. It seems to me there may be
25 something here and but we don't really know.

1 But it doesn't mean that we conclude the opposite,
2 that there isn't something. I think that would be an
3 under-interpretation of the study.

4 DR. FUCALORO: Yeah. But also an interpretation
5 is that MITC extends the life of the rats, if you look at
6 some of these. So one has to wonder.

7 CHAIRMAN FROINES: But there are people, lot of
8 people who do studies like this, like Maltoni, who doesn't
9 sacrifice the animals at 104 weeks, but actually carries the
10 studies out until a later date when the animals are dying,
11 and actually that's where you actually tend to find more
12 tumors when you go beyond the 104 week, two-year period. So
13 one could argue that the danger of a shortened study, of
14 course, is that you don't see the cancers, because cancer is
15 a late-stage event. You pick 104 weeks because that's when
16 they're old. It's like picking -- it's like waiting until
17 we're 65 and seeing if we have cancer cells. We might have.
18 We will have more by the time we're 80. So we do need to be
19 careful about our interpretations.

20 DR. FRIEDMAN: Can I add one?

21 Stan probably could figure this better than I can,
22 but when I look at this Fisher test you did on the very
23 bottom line that gave you .007.

24 DR. RUBIN: Yeah.

25 DR. FRIEDMAN: 36 over 60, compared to --

1 DR. RUBIN: No. The way I took the very highest
2 incident rate, the one that's underlined there, 30 over 60
3 versus 44 over 60.

4 DR. FRIEDMAN: I don't think that's quite cricket
5 to look at the data and then pick the one you wanted to
6 test.

7 DR. RUBIN: I wanted to give it the most
8 possibility of seeing something.

9 DR. GLANTZ: I think, I'm just sitting here doing
10 a lot of arithmetic, if you take the -- if you look at the
11 top at the terminal survivors and you add the multiple --
12 the thing John said, you add the multiple plus single
13 fibroadenoma with the carcinomas, and you just looked at
14 exposure, versus unexposed, which I think makes more sense
15 when you look at these numbers, that is probably
16 statistically significant. And, I mean, I think that if you
17 look at the multiple fibroadenoma and you just looked at
18 exposed versus unexposed, that's going to be significant.

19 DR. FRIEDMAN: Again, you're doing that after you
20 see the data.

21 DR. GLANTZ: Well, that's true but, you know, hey.
22 That doesn't bother me.

23 DR. FUCALORO: You've got to make a point.

24 DR. GLANTZ: I agree, picking out the highest
25 incident rate, you don't want to go do that, but I think

1 that if you look at the data and you do a test of the
2 trends, the test of the trends aren't significant, but if
3 you look at the numbers, the reason it's not significant it
4 looks like there's a threshold effect that you get exposed
5 and something happens and if you got even more exposure, you
6 don't seem to be getting a larger effect.

7 Now, whether that's because there was some enzyme
8 that saturates and whether that's because the rats won't
9 drink the water, you don't know. But if you just divide it,
10 if you collapse the categories, then the first one will be
11 much more significant, I think.

12 I don't have a statistical table here and this
13 doesn't take a square root, so I was sort of having to guess
14 a little bit.

15 I think if you look at the multiple plus single
16 fibroadenomas, that probably doesn't reach significance, but
17 you'd get a smaller P value than you have there, but if you
18 add the carcinomas with the fibroadenomas, that gives you a
19 Z of like 1.9, which is right on the border.

20 And probably if you do a Fisher exact test it
21 would be significant.

22 So, you know, the interpretation I would put on
23 this stuff is that it looks like you're showing that
24 exposure is associated with an increased tumor rate.

25 DR. FRIEDMAN: And having seen that in this study

1 it would be really nice to do another study with that
2 hypothesis in mind. If that were at all possible, that
3 would be wonderful.

4 DR. RUBIN: \$1.5 million.

5 DR. FRIEDMAN: I'm in the wrong business.

6 DR. RUBIN: Can I move on?

7 CHAIRMAN FROINES: I want to ask --

8 DR. GLANTZ: This is turning into a seminar here.

9 Is this your thesis you're defending here?

10 CHAIRMAN FROINES: But this is important.

11 Although I don't think that the determination of
12 these compounds as TACs rests on oncogenicity issue.

13 I think this is something that clearly requires
14 follow-up, something that for which there are hints, but for
15 which there is no defined --

16 DR. GLANTZ: But I think the data here are strong
17 enough to say that's there's, at the very least, a strong
18 suggestion of an effect.

19 DR. BYUS: I wouldn't say that at all.

20 DR. GLANTZ: You don't?

21 DR. BYUS: No. I would say you cannot say -- I
22 would not say it indicates a strong --

23 DR. GLANTZ: No, I would say --

24 DR. BYUS: I would say there is maybe an effect.

25 DR. GLANTZ: Okay.

1 DR. BYUS: It's definitely not a strong effect
2 from this data.

3 DR. GLANTZ: No, no. I said --

4 DR. BYUS: You said strong effect.

5 DR. GLANTZ: No, no. I said strong suggestion.

6 DR. FRIEDMAN: I would take out the word strong.

7 DR. GLANTZ: Okay.

8 DR. FRIEDMAN: It's suggestion of an effect, it
9 should be followed up.

10 CHAIRMAN FROINES: If you want, we'll work on this
11 in terms of our findings and we'll have to resolve this
12 strong suggestion versus the suggestion.

13 DR. GLANTZ: How about a somewhat moderate --

14 CHAIRMAN FROINES: Somebody in this room, who is
15 very articulate, start thinking of the term between strong
16 suggestion and suggestion.

17 DR. BYUS: Stan and I can go out of the room.

18 DR. GLANTZ: No, no.

19 DR. KENNEDY: Real suggestion.

20 DR. GLANTZ: A moderate suggestion.

21 CHAIRMAN FROINES: All right. We'll come back to
22 that.

23 DR. GLANTZ: Somewhat stronger suggestion,
24 perhaps, an apparently somewhat strong suggestion.

25 CHAIRMAN FROINES: Bang, bang, bang, bang, bang.

1 DR. BYUS: Where is your gavel?

2 DR. GLANTZ: We're not allowed to joke.

3 CHAIRMAN FROINES: I have a question. I want to
4 get back to science.

5 The second study, the mouse study, the reason I
6 want to ask a question about the mouse study is that the
7 principal findings of angiosarcoma in the metam-sodium is in
8 the mouse, not in the rat.

9 DR. RUBIN: Right.

10 CHAIRMAN FROINES: Now, in the mouse study here I
11 didn't understand this paragraph. You said in a two-year
12 oncogenicity, 70 mice, blah-blah-blah, blah-blah, but I
13 couldn't tell what was the size of each group, it looked to
14 me like the size of each group was six.

15 DR. RUBIN: 70 mice per group.

16 CHAIRMAN FROINES: This says 70 mice per sex, per
17 group, but then on the back you're seeing things like
18 ovarian cysts were increased in 10 of 21 versus 2 of 21, so
19 that without having a table --

20 DR. RUBIN: That's the death problem.

21 CHAIRMAN FROINES: I don't know what the size -- I
22 have no idea how to interpret this study, because there's no
23 data. I see six mice from each group were sacrificed at 26
24 and 52 weeks. So was the study terminated at 52 weeks? No?

25 DR. RUBIN: No.

1 CHAIRMAN FROINES: It was terminated at 104 weeks.
2 These are mice, so how long, 18 months?

3 DR. RUBIN: Usually run an 18-month study with
4 mice. I suspect the animals were dying and what you're
5 seeing are the ones that are left.

6 CHAIRMAN FROINES: There's really not enough
7 information in this section to interpret this study, and
8 it's important precisely because you want to look at this.
9 Again, the strains are different, conditions are different
10 from the metam-sodium study, but if you want to look at
11 mouse-to-mouse findings, you need to have the information to
12 better understand what was done.

13 You see what I'm saying?

14 DR. KENNEDY: I see. I don't think it's going to
15 change the oncogenic --

16 CHAIRMAN FROINES: I don't think so either.

17 DR. KENNEDY: -- endpoint. In terms of animals, I
18 think many strains of mice, if they live long enough they
19 all die eventually.

20 DR. WITSCHI: No. I think the question about the
21 mice is very important, because Andy has taken a positive
22 mouse study to ascertain the data which are as weak perhaps
23 as metam-sodium as they are from MITC. But this was your --
24 made your decision swing. And he calls metam-sodium a
25 carcinogen with lousy rat data and the positive mouse study.

1 And he calls the MITC not a carcinogen with lousy rat data
2 and not positive mouse data. So they have a good --

3 DR. RUBIN: We're whistling a slightly different
4 tune on the next slide. I think some of the language I've
5 heard here is reflected in the next slide as to what the
6 conclusion of the onco study is.

7 Here I just list some of the arguments for and
8 against considering a MITC -- an oncogen based on this one
9 study. I don't know if you want me to go through these, but
10 I'll read the conclusion first.

11 There is weak evidence of a possible treatment
12 effect. However, the data are not sufficiently strong to
13 trigger a quantitative oncogenic risk evaluation. That is
14 what I mean by that is plugging data like 50 percent versus
15 70 percent into a multistage linear extrapolation program
16 because the data won't mean anything.

17 However, I think we have come to the conclusion in
18 our branch that these data, particularly on fibroadenoma,
19 are possibly consistent with the treatment effect. And
20 that's all I think you can say at this point.

21 So I am going -- I'm changing the language,
22 because the language in the document, as you have it now, is
23 there's no clear effect of oncogenicity. I'm going -- I
24 think the language really should be something like what I
25 have here or some other language that you would suggest.

1 DR. WITSCHI: I think that's reasonable. We're
2 talking about, I mean the data are so expensive, something
3 seems to be there, but nobody in his right mind should use
4 this study to a quantitative risk assessment.

5 CHAIRMAN FROINES: We just gave Craig his piece of
6 this action, so it's okay.

7 DR. RUBIN: We've discussed everything on this
8 slide. I think we can move on.

9 DR. WITSCHI: I might remind Craig that absence of
10 evidence is never evidence for absence.

11 DR. BYUS: Absolutely.

12 DR. GLANTZ: It's noon, if you expect Blanc to
13 show up at 12:30, maybe we should take lunch.

14 CHAIRMAN FROINES: 1:00.

15 DR. GLANTZ: 1:00, okay. I'm sorry.

16 CHAIRMAN FROINES: Why don't we stop about 12:15
17 and we will come back at 1:15.

18 And, you know, I don't want to make too much of
19 having one person, because this discussion has been quite
20 good. Everybody has participated.

21 DR. GLANTZ: Yeah, since Paul is going to show up,
22 it would be good not to have him watch us eat lunch.

23 But, anyway, go on.

24 CHAIRMAN FROINES: I think there's a general
25 consensus, there might be slight wording differences, but I

1 think there's a consensus here that there is a suggestion
2 that something is happening. The data is not sufficient to
3 use for risk assessment purposes. And that we all, I think,
4 agree further work should be done.

5 So go ahead. Why don't we proceed.

6 DR. RUBIN: Next slide.

7 Now we'll get to shift gears and come to the risk
8 characterization part of this document.

9 Just to refresh your memory, we have split this,
10 these exposure and risk calculations, into acute and
11 subchronic or seasonal exposures and then each of those
12 categories are split into ambient exposures and that would
13 be defined as exposures of the general public in the general
14 area where metam is being applied, so that would be
15 exposures in town, small townships and so forth, versus
16 off-site, or perhaps a better term now, application site
17 exposures, these would be people that are standing right off
18 the field in a particular exposure scenario.

19 And I want to just give you the MOE values, the
20 margins of exposure. A margin of exposure is defined as the
21 NOEL, in this case for acute we're setting the NOEL at 220
22 ppb, divided by the measured air concentration. So the MOE
23 is a value which expresses just how close to the NOEL a
24 particular air concentration is. The lower the MOE, the
25 more reason for concern.

1 What we have here are the high acute MITC exposure
2 levels for these various townships and houses and outside of
3 houses and in the general environment, four or five
4 different townships.

5 We get MITC levels. I think Tom Thongsinthusak
6 can comment better on this, but we get MITC levels ranging
7 from .08 ppb all the way up to almost 9 ppb with a
8 corresponding MOE values ranging from 25 to 2,750.

9 Since these MOEs are based on human data, the
10 benchmark of concern is an MOE of ten. So for at least at
11 this point, ambient exposures, that is exposure in town, in
12 a season of metam application, is not ringing a bell, not
13 raising a flag.

14 However, next slide, for the off-site or
15 application site measurements, you get much higher MITC
16 levels if you're standing five to 500 meters from a field
17 where metam is being applied. Using the same NOEL value of
18 220 ppb, we're getting MOE values less than one in many
19 cases, and certainly all ten or less.

20 These are --

21 CHAIRMAN FROINES: In the previous slide, the Kern
22 County, I take the '97, '98, that's Jim Seiber's work;
23 correct?

24 DR. RUBIN: Right.

25 CHAIRMAN FROINES: Okay. When he did that, did he

1 look -- did he estimate the MIC or carbon disulfide or any
2 other breakdown products?

3 DR. RUBIN: I don't think MIC was estimated in
4 that study, but there might be others.

5 Our exposure people are saying no.

6 CHAIRMAN FROINES: So that we may have half a loaf
7 here or a ten percent or 90 percent of a loaf.

8 DR. RUBIN: We need monitoring data on these
9 breakdown products.

10 What I'm going to give you here are just MOEs for
11 MITC.

12 CHAIRMAN FROINES: And the MITC on page nine that
13 you're at now, that also doesn't include MIC?

14 DR. RUBIN: Apparently not.

15 But even not considering MIC, we're dealing with
16 MOE values that almost certainly indicate that a person
17 standing next to a field when there's spraying going on
18 where there's chem irrigation that is adding metam into the
19 irrigation water or shank injection, that there's going to
20 be at least eye irritation going on out there, and that's
21 what these MOE calculations are telling us.

22 And there could well be pulmonary effects.

23 Next.

24 These are, I'm flooding you with numbers. You
25 don't of course have to read every number in this chart.

1 CHAIRMAN FROINES: When was the previous slide
2 collected?

3 DR. RUBIN: Excuse me?

4 CHAIRMAN FROINES: The previous slide, when was
5 that was data collected?

6 DR. RUBIN: These are the off-site acute
7 measurements. I have them in the document.

8 CHAIRMAN FROINES: I don't want -- I'm trying to
9 avoid flipping back.

10 FROM THE AUDIENCE: 1993, '94 and '95 --

11 DR. RUBIN: That's right. '93, '93, '95, '93,
12 '92.

13 CHAIRMAN FROINES: And use of metam-sodium has
14 gone up since that time?

15 DR. RUBIN: It's about doubled.

16 CHAIRMAN FROINES: About doubled?

17 DR. RUBIN: Yeah.

18 MR. GOSSELIN: Also that kind of changes, the use
19 has gone up, but in '94 we started a series of changing use
20 practices, so how this data fits with what's going on now is
21 something we're taking a look at.

22 DR. FRIEDMAN: Question about similar to my
23 questions about your P values, when you show the MOE, why do
24 you say less than one, why don't you pick the actual value,
25 because .9 would be a lot different than .1.

1 DR. RUBIN: Yeah, I can do that. You're right.
2 These already when you're dealing with MOE values of one or
3 less, you're dealing with almost certainly seeing adverse
4 effects. So to me it simplified it just to say they were
5 less than one. You can do the division right out here. I
6 mean, the numbers are, for instance, for site A, injection,
7 220 divided by 618, so it would be .3, approximately.

8 Would you suggest that I do that?

9 DR. FRIEDMAN: I would think that it would be
10 good. Shouldn't require the reader to have to do it.

11 DR. RUBIN: Okay.

12 DR. FUCALORO: You can also put in the range too.

13 DR. RUBIN: Yeah, right.

14 CHAIRMAN FROINES: I think we should break now.
15 This probably is a reasonable time, because it might be good
16 for Paul to see some of this too.

17 It's going very well.

18 (Thereupon the lunch recess was taken.)

19

20

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25

1 A F T E R N O O N S E S S I O N

2 CHAIRMAN FROINES: Go ahead.

3 DR. RUBIN: Dr. Froines asked me to go back to
4 page nine, start up there.

5 This was the exposure in the MOE calculations for
6 the application site or off-site measurements, five
7 different studies, three of them injection studies or
8 injection applications, and two of them sprinkler
9 applications.

10 And the point of this slide was to show that when
11 you're standing right off of a field in which metam is being
12 applied, you're very high likelihood of sustaining some of
13 the irritation effects. The MOEs are less than one. It was
14 mentioned in the last session that I should perhaps express
15 the exact MOE instead of just less than one. We'll probably
16 do that.

17 Are there any more questions on this slide?

18 One issue came up, I was told site C, there was
19 MIC monitoring in the site C study. That's the one study in
20 which there is --

21 DR. ATKINSON: This was the '95 Kern County one, I
22 assume?

23 DR. RUBIN: Yes.

24 Okay. Next slide.

25 Now we move on to the risk characterization for

1 seasonal exposures. The NOEL value used here for these MOE
2 calculations is derived from the 12-, 13-week rat inhalation
3 toxicity study. The endpoints were in that study, just to
4 refresh you, were decrements in weight gain, increased water
5 consumption and decreased serum protein.

6 And here these are the ambient MOE levels. And
7 you can see that they're not tripping any red flags.
8 They're all quite fairly high, ranging from low of 708
9 calculated for children at Lamont, to as high as 17,000 at
10 Arvin, calculated for females. The Lompoc measurement
11 there, the 3.4 million, I was told that maybe I shouldn't
12 emphasize that. We're not so keen on the reliability of
13 that data, so I'm going to cut back on that.

14 The next slide finally is the -- are the MOE
15 calculations for off-site exposures for seasonal exposure.
16 And here we get MOEs as low as two, ranging as high as a
17 mean MOE of 236.

18 Now, for MOEs calculated based on animal studies,
19 the benchmark or the convention for tripping a health
20 concern is a MOE of a hundred. These are clearly coming in
21 below a hundred.

22 DR. BLANC: Therefore, even if you had
23 overestimated exposure by a factor of five to ten, you would
24 still be triggering --

25 DR. RUBIN: That's right.

1 DR. BLANC: Do you think that is significant?
2 Does that reassure you that even if there was some error in
3 the field measurements that even so you would have such a
4 high margin here in terms of your MOEs that even if you had
5 overestimated field exposure by a factor of five to ten --

6 DR. RUBIN: I would still be concerned, yes.

7 DR. BLANC: Right.

8 DR. RUBIN: However, I'll just remind you that
9 there is significant concern about the endpoints in the
10 particular study. I would love to see this study done again
11 in a properly characterized analytical procedures, the
12 analytical chamber concentrations, all the individual animal
13 data expressed. We're forced into a corner on this study.
14 We have to go with it. We don't have anything better at
15 this point.

16 So it is possible that a well-characterized study
17 will come up with a higher NOEL value, in which case these
18 MOE values are going to be higher.

19 DR. BLANC: Of course, it's also possible a
20 well-characterized study would come up with an even lower --

21 DR. RUBIN: Yes, certainly is.

22 CHAIRMAN FROINES: There is some indication that
23 based on George's paper and the Dunsmuir that you might find
24 exposures over time of relatively low levels according to
25 your document.

1 DR. RUBIN: Yeah. There is uncertainty in all of
2 these calculations and some major uncertainties.

3 Next slide.

4 We have calculated reference exposure levels.
5 These are as --

6 CHAIRMAN FROINES: Just one comment. I think,
7 Paul, that the other thing that's missing here that you
8 missed in earlier discussion is none of this includes MIC
9 carbon disulfide, H₂S.

10 DR. BLANC: That was the case.

11 CHAIRMAN FROINES: This is only MITC.

12 DR. BLANC: Yeah.

13 CHAIRMAN FROINES: So depending upon how much of
14 that would be produced, MOE, however one would calculate it,
15 would be different.

16 DR. RUBIN: Okay. Just we have calculated
17 reference exposure levels for acute toxicity since we
18 have -- we're dependent on a human study, eye irritation
19 study, the reference exposure level is calculated by
20 dividing the NOEL by ten.

21 And when you do that, when you divide 220 by 10,
22 you get 22 for a reference exposure level. And it's quite
23 instructive now to compare that reference exposure level to
24 the actual measurements of MITC both in ambient and off-site
25 studies.

1 The ambient does not appear to go above the
2 reference exposure level. Those, say, in town around in a
3 season of application. However, the off-site, the mean
4 values never go below the REL, so that is an area for
5 concern.

6 Okay. Next slide.

7 Reference exposure levels for the subchronic is
8 equal to the NOEL divided by a hundred and that's because
9 the subchronic NOEL comes from an animal study.

10 CHAIRMAN FROINES: What happens if you were to
11 calculate in a REL for children?

12 DR. RUBIN: For acute or subchronic?

13 CHAIRMAN FROINES: I'm using acute.

14 DR. RUBIN: What we have made, I don't know
15 whether to call it an assumption, but an irritation -- we've
16 made the assumption that irritation in children, female
17 adults and male adults is going to be the same. In other
18 words it's not being -- it's not being metabolized, there's
19 no breathing rate considerations here. So we have assumed
20 that the effect on children of this irritation endpoint is
21 going to be similar to that on adults.

22 DR. BLANC: Although to the extent that children
23 would be more symptomatic or more sensitive, you're taking
24 that much into account with a factor of ten, even with the
25 human data.

1 DR. RUBIN: Right.

2 DR. BLANC: It does assume that there are
3 sensitive subpopulations within the whole population.
4 Otherwise, you'd have to assume that children were a
5 separate population and then do another division for
6 sensitive children. So that would be an unusual -- it would
7 not be a standard approach. The factor of ten is taking
8 into account that children may be somewhat more responsive
9 as a subpopulation.

10 DR. RUBIN: If there are any literature out there
11 that would indicate that children are more sensitive with
12 respect to irritation endpoints, I'd certainly be interested
13 in it.

14 CHAIRMAN FROINES: There may be to the degree that
15 one thinks about micro-environmental monitoring, there may
16 be some potential to dermal absorption in children that
17 might be different.

18 Go ahead.

19 DR. RUBIN: Okay. The reference exposure for
20 subchronic toxicity is the NOEL divided by a hundred. This
21 is because the NOEL was determined in an animal study, so we
22 have uncertainties of ten for both the human range of
23 sensitivities and going from animals to humans.

24 The way we do this is to calculate from the rat
25 NOEL what I would call a human equivalent NOEL, which takes

1 into account the different breathing rate of humans, in this
2 case human children, compared to rats, and amortizes the
3 data. This particular experiment the exposures were done
4 only five out of seven days, and only four hours out of
5 every 24 hours.

6 All these modifying factors changed the NOEL, the
7 rat NOEL, which was one ppm in the rat to a NOEL of 0.1 ppm
8 in humans, and dividing that further by a hundred gives us a
9 REL of 1.5 ppb. This is subchronic REL.

10 And in the document you'll notice that I've also
11 calculated a chronic REL by dividing further the subchronic
12 REL by another factor of ten. I don't think OEHHA does
13 that, and that I'm very open to comment. Perhaps a factor
14 of ten is not appropriate.

15 DR. BLANC: Where did that ten come in again? I'm
16 sorry.

17 DR. RUBIN: Because we want to generate a chronic
18 REL value, but we only have a subchronic study.

19 DR. BLANC: Right.

20 DR. RUBIN: So there's another factor of ten
21 uncertainty.

22 DR. BLANC: I see. I see. Okay.

23 DR. RUBIN: So we get a chronic REL of 0.1 ppb.

24 Okay. I'll finish the talk with just a couple of
25 slides on the alternate or the other breakdown products.

1 Methyl isocyanate is an extremely toxic compound.
2 I don't think I need to say that. It killed on the order
3 of, say, anywhere from 2500 to 5,000 people at Bhopal in two
4 or three days, maybe five days.

5 So this compound has a real good track record for
6 toxicity.

7 We have up to this point only one monitoring study
8 which tracks MIC. In that study there was one spike of MIC
9 as high as 2.5 parts per billion, which was about four
10 percent of the MITC that was there.

11 Now, that, I suspect, may be a high estimate of
12 the amount of MIC around, but we definitely need, in my
13 opinion, to have more data on the amount of MIC around when
14 there are metam applications going on.

15 MIC, I've just listed here are the LC 50s in
16 animals 6, 12 and 5 in rats, mice and guinea pigs. These LC
17 50s are quite a bit lower than MITC. This is a more acutely
18 toxic compound --

19 DR. BLANC: By a factor of ten?

20 DR. RUBIN: Ten to hundred.

21 DR. BLANC: It's not in here, the LD 50, in this
22 little handout

23 DR. RUBIN: For MITC, no, it's not in there, no.

24 DR. BLANC: But it's one to two orders of
25 magnitude?

1 DR. RUBIN Yeah.

2 DR. BLANC: Like two orders of magnitude.

3 DR. RUBIN: Yeah.

4 CHAIRMAN FROINES: Can I ask you a question? You
5 have the acute LOEL of one part per million.

6 DR. RUBIN: Yeah.

7 CHAIRMAN FROINES: But in the document, for
8 example, you have a ten-minute study at .5 part per million
9 found eye irritation, tearing, nose and throat irritation,
10 and so that would seem to indicate that you have a LOEL at
11 .5 part per million and then down here below that in the
12 Allory studies you have certainly a LOEL of 1.3 part per
13 million, increase in respiratory rate, and I didn't look at
14 the paper, but I don't know whether he saw anything in lower
15 dose than 1.3 part per million.

16 But it seems like given this ACGIH information,
17 one could suggest a lower LOEL than one part per million,
18 based on what you have in your document.

19 DR. RUBIN: I'll definitely go back and look at
20 that.

21 CHAIRMAN FROINES: I'm just reading what you
22 wrote.

23 DR. RUBIN: You're absolutely right.

24 DR. BLANC: Well, another way of asking the same
25 question, I think why John is a little taken aback is

1 because typically the lethal concentration was six parts per
2 million, and in five parts per million you wouldn't expect
3 the LOEL to be one part per million. It's very steep --
4 it's possible, but --

5 DR. RUBIN: It could be that -- I have to go back
6 and look. It could be that those are air concentrations, in
7 which case they're very different.

8 DR. BLANC: That would be more relevant to our
9 concerns.

10 DR. RUBIN: Exactly.

11 DR. BLANC: Do you remember the lethality studies
12 well enough to have a sense of what the curve looked like in
13 terms of mortality?

14 DR. RUBIN: I couldn't comment on that.

15 CHAIRMAN FROINES: The document has a LC 50 at 6.1
16 ppm.

17 DR. BLANC: He's got at the top here 6.1 ppm in
18 rats and 5.4 ppm in guinea pigs.

19 And I don't know whether that's because they saw
20 no lethality at .5 parts per million or -- in other words,
21 if they saw 15 percent mortality at one part per million,
22 you hardly call that a no effect level.

23 So maybe there's some information in the LC 50
24 studies that would be -- would take your LOEL lower than
25 just by looking at it from that point of view. I don't know

1 what the studies were.

2 CHAIRMAN FROINES: But the ACGIH study did find,
3 according to this, ten minutes at .5 ppm eye irritation, and
4 so you may find when you look at that, that data you
5 described may be awfully limited, would be my guess.

6 DR. RUBIN: Yes.

7 DR. BLANC: Wasn't there also some modeling data
8 from Bhopal?

9 DR. RUBIN: What the concentrations were?

10 DR. BLANC: Yeah. From the various plume radiuses
11 and when they no longer saw any symptoms.

12 DR. RUBIN: There was modeling data from Bhopal.
13 There are estimates of the concentrations, that the max
14 concentrations that would have been experienced around the
15 factory, but I don't know how sophisticated it was. I have
16 some of those estimates in this document.

17 DR. BLANC: Because you want us to make sure that
18 you were being consistent, that it seemed consistent, and
19 you didn't have an estimate that at two miles there's a
20 concentration of .5 ppm and that's where people were having
21 just eye irritation and all that stuff, and then we're sort
22 of arguing against the LOEL.

23 CHAIRMAN FROINES: The other point I would make
24 here is, and I don't know what you can do with it, if
25 anything, but this data on pregnant mice --

1 DR. RUBIN: Yeah.

2 CHAIRMAN FROINES: -- where you say that exposure
3 of pregnant mice for six hours per day on gestation days,
4 but increased mortalities over control and fetuses at one
5 and three parts per million.

6 So you're seeing more lethality, embryo lethality,
7 at one part per million, but that's an interesting question
8 about whether you would use a safety factor of ten to get
9 you to a NOEL, when you have such a profound effect.

10 What would you use?

11 Anyway, let's let it go, because that's a LOEL of
12 one part per million, but that seems pretty high.

13 DR. RUBIN: Yeah. That's what I used as the LOEL.

14 CHAIRMAN FROINES: But to take a factor of ten
15 below that for your NOEL, with that endpoint I'd be nervous
16 about it, frankly.

17 DR. RUBIN: So you would --

18 CHAIRMAN FROINES: I think you'd see more
19 lethality -- well, I don't know, it's hard to say. Again,
20 it's Paul's point about the shape of the dose response
21 curves.

22 DR. RUBIN: Okay. Well, using a LOEL of one ppm,
23 I calculated some conditional acute RELs for a one-hour,
24 six-hour, 24-hour exposure, coming up with the numbers you
25 see on the screen, 14.2, 2.4 and .6.

1 There's a mistake in the document. I had made the
2 calculation in the document based on rat breathing rates,
3 and these are actually mice in the experiment. So that's
4 why the numbers look a little different than they do in the
5 document.

6 DR. FUCALORO: These are just purely
7 proportionate?

8 DR. RUBIN: Yes. These are based on a Haber's Law
9 proportionality.

10 DR. FUCALORO: With a exponent of one?

11 DR. RUBIN: N equals one, yeah. I used N equals
12 one. OEHHA in their acute hot spots document lists a number
13 of end values for MIC irritation values. They range from .5
14 to 1.1. And I thought just to use one, it will be just a
15 straight proportion, Haber's Law proportionality, and in
16 extrapolating from six to 24 hours and from six to one hour.

17 As I said before, the MIC level, the high MIC
18 level, measured after one metam -- after an metam
19 application i one study, was 2.5 ppb. Clearly we're in that
20 range just for the acute, for these conditional acute REL
21 values.

22 I just listed some of the NIOSH values here. The
23 TLV, the eight-hour PEL, based on corrosivity and reactivity
24 of 20 ppb, which is somewhat higher than the values that
25 I've calculated here.

1 DR. BLANC: They shouldn't be, because they
2 intentionally don't take into account any susceptible
3 populations.

4 DR. RUBIN: Right. These are workers.

5 DR. BLANC: If it were any lower than that, you'd
6 really worry since you will --

7 DR. RUBIN: About child labor laws?

8 DR. BLANC: You should at least be ten times lower
9 than that, at least, depending on how it's done, quite a bit
10 lower than that, but at a minimum.

11 DR. RUBIN: Right. I don't have any eight-hour
12 type of value here, because -- well, no, take it back. I do
13 have a six-hour value here and it's getting down toward
14 one-tenth that of the NIOSH value.

15 The other byproduct or degradation product of
16 great concern is hydrogen sulfide. This we have -- you can
17 fill this room with books written on toxicology of hydrogen
18 sulfide. It's one of the most, if not the most, toxic
19 industrial gas out there.

20 There's a fair amount known about the levels of
21 sensitivity in human populations, getting respiratory
22 irritation at 100 ppm up to cardiovascular arrest and death
23 at 700 ppm.

24 For these values, I pretty much relied on the
25 ATSDR values that for a minimum -- what's MRL stand for?

1 Minimal risk level. An acute minimal risk level of 70 ppb
2 and subchronic minimal risk level of 30 ppb.

3 In the monitoring that we've -- that we have so
4 far, we do see levels rising above those MRLs at one to four
5 hours, 76 ppb, and then going down with hydrogen sulfide.

6 I suppose one always has to be worried that there
7 are other sources, plenty of other sources of hydrogen
8 sulfide in the atmosphere, so while it does appear to be
9 going down, perhaps the reason it's coming back up into
10 detectability ranges is that there's some other source
11 there. I really don't know.

12 The real problem that we're up against here, in my
13 opinion, is how would we go about doing a combined
14 assessment, in other words MITC plus some average or some
15 level, some high level of hydrogen sulfide or MIC, and that
16 I think is quite a cutting-edge issue in risk assessment.

17 I don't have any answers for that right now. I've
18 based this whole assessment on MITC alone, recognizing that
19 hydrogen sulfide levels are high enough to be of concern and
20 MIC levels are certainly high enough to be of concern in
21 their own right, totally apart from whether they're
22 appearing in conjunction with MITC.

23 There are a few other degradation products,
24 including carbon disulfide, which are monitoring in the one
25 study that I know of, our monitoring has not indicated

1 detectable levels. Also carbonyl sulfide and methylamine,
2 which I don't think we have any monitoring data on.

3 DR. WITSCHI: I have a question or a suggestion to
4 your question about different things being present. As far
5 as MITC is concerned, some of the ambient levels of it were
6 closer about the RELs, right?

7 DR. RUBIN: Yes.

8 DR. WITSCHI: So these were levels which
9 presumably, accordingly to our business should have done
10 something, and they can also be assumed that people at this
11 time are exposed not only to MITC, but to MIC and sulfur.

12 Do we have any complaints or do we have any data
13 on people getting sick?

14 DR. RUBIN: We do have a -- we have a program
15 called PISP, Pesticide Illness Surveillance Program. And
16 I've got some of that data in the risk assessment as
17 recently as we have it, and there are indeed injuries in the
18 field with metam applications.

19 DR. WITSCHI: Those data be complete enough at
20 least to give you some clues as to what multiple exposure
21 would mean?

22 DR. RUBIN: I would say there's probably not
23 enough there to make any conclusions about response --

24 DR. WITSCHI: Not so much conclusion as
25 hypotheses.

1 DR. RUBIN: I'm a good speculator. Sure. There's
2 certainly a possibility here that some of the other
3 degradation products could be responsible.

4 DR. WITSCHI: To say that really strikes me. This
5 whole thing is we often construct some hazards or risk
6 assessments from animal toxicology, but we do not very often
7 have a chance to verify what the animal tells us about human
8 data. And maybe this might be one of those situations.

9 MR. GOSSELIN: Maybe this might answer your
10 question. Is your question have we been seeing incidents
11 from metam-sodium applications where people have been
12 complaining for exposure to -- we're not going to know
13 exactly what they were exposed to.

14 DR. WITSCHI: Well, yes, my question really was
15 this seems to me, given exposure data and the possibilities
16 of exposure where there seems to be a real possibility that
17 human data are out there which would reinforce what we
18 conclude from the animal studies, and, if so, that could be
19 very very closely looked at.

20 MR. GOSSELIN: Actually, that's been one of the
21 things we've been chasing for a number of years is incidence
22 from workers and also incidence from off-site ambient air
23 samples. And it's caused over the years, most specifically
24 since '93-94, alterations to what practices be allowed to
25 happen. Some of these are occurring from legal applications

1 and then some are misused, but sort of the effects of the
2 exposures, what we have the evidence on.

3 DR. BLANC: In fact over half of the cases
4 reported to the pesticide and surveillance network have been
5 nonoccupational ambient cases; right?

6 So that's a ratio which I would imagine is higher
7 than the ratio of ambient to -- or drift, let's say, because
8 I don't want to say occupation, because a lot of other
9 pesticides it's not optional, but it is application driven,
10 but that's fairly high ratio it would seem to me, other than
11 the ratio by standard complaints, because of petroleum
12 distillate smells or something. But that's sort of very
13 strongly supportive of what Hans was saying, the fact you
14 have a lot of evidence that there is a toxic air problem
15 with this, at least in the acute arena.

16 DR. FUCALORO: Can I follow up on what Hanspeter
17 was saying?

18 When you get something reported in your
19 surveillance program, how much information is reported? How
20 much are you trying to get? Do you get, for example, the
21 length of time of exposure, estimated concentrations and the
22 illness or the effect? In other words, is there something
23 quantifiable, is it possible to get aggregate data and do
24 something quantifiable? I don't know.

25 MR. GOSSELIN: There's a wide range of data that

1 comes through the illness surveillance program. Some of it
2 lags a long time because we get what's called doctor's first
3 reports. Some of you may deal with that. If you suspect
4 it's a pesticide illness or exposure, you're required to
5 report that in to the Department of Industrial Relations and
6 we get that and we'll have staff review that and try to
7 categorize what went on.

8 Other times there are incidents that are directly
9 reported to us and we conduct an immediate investigation
10 with the counties to, one, not only categorize what the
11 exposures were and what occurred, but also to determine if
12 there were violations that occurred under our normal
13 enforcement and surveillance program.

14 DR. FUCALORO: I understand all those things.

15 MR. GOSSELIN: Here's kind of what you are asking
16 about, looking at sort of trends and issues, what we've
17 found oftentimes, particularly with agricultural workers
18 reentering fields, sometimes there's trends that occur about
19 from a variety of effects that are illustrated in the data
20 showing a certain crop using a certain material and the time
21 that's elapsed before people go in that causes us to go in
22 and have to extend that time to allow the degradation of the
23 material to occur. That data, that illness data, has also
24 been used to fix some of those problems.

25 DR. BLANC: In fact, if we go back to the usage

1 data that we discussed at a previous meeting, where there
2 was a sharp upswing in pounds applied in 1994, 1995, is that
3 right? Do I have the year right?

4 DR. RUBIN: My recollection of the data was that
5 from '91 to '98 the -- well, from '91 to '95 the use rate
6 doubled, and so that's what we know.

7 DR. BLANC: In fact, beginning in 1995 you have a
8 two- to fourfold increase in the number of reports of
9 drift-related events?

10 DR. RUBIN: Right. And that's directly --

11 DR. BLANC: Wouldn't that support the -- wouldn't
12 those observations of ecological data support the hypothesis
13 that metam-sodium and its breakdown products are causing
14 ambient air problems in California?

15 DR. RUBIN: I would definitely agree with that.
16 The use went up and the ambient incidence went up.

17 DR. BLANC: If you only had the pesticide
18 surveillance program data and none of the elaborate animal
19 data that you have, would that alone be enough to support
20 considering this material toxic as an air contaminant?

21 MR. GOSSELIN: It --

22 DR. BLANC: I don't mean from a strictly
23 regulatory point of view, but from a sort of common sense,
24 public health regulatory point of view.

25 MR. GOSSELIN: I think so. And I think the way

1 that a lot of the counties that have been facing incidents
2 that are occurring, that's the way they have reacted. You
3 know, there's been a lot of issues about the eye irritation,
4 eye blink. This a traditional toxic effect.

5 The fact of the matter is regulators are going to
6 do we need to solve that problem so that the phone calls
7 don't come in and people don't complain. I think back in
8 '97, beyond what things we had put out, '94 Kern County, I
9 think, moved on their own, any application outside of the
10 city limits, because they went through and started seeing
11 where they were getting complaints historically, it was all
12 within city boundaries, and on their own made a policy, I
13 think, to move everything outside.

14 DR. BLANC: Is that historical event documented in
15 your human health assessment section?

16 MR. GOSSELIN: I don't think a lot of --

17 DR. BLANC: Is that too anecdotal?

18 MR. GOSSELIN: It gets into, I think, some of the
19 risk management things that have been done out in the field
20 that's probably not captured to a great extent out here, I
21 mean in this document.

22 DR. RUBIN: I just have a conclusion slide.

23 CHAIRMAN FROINES: Going back to Bob Spear's
24 presentation about the variability of exposure estimation,
25 it's interesting, because this data here for '95 and '96 is

1 so striking, recognizing that variability it again goes to
2 this issue of whether or not MOEs is the way to determine
3 whether something should be clarified a toxic air
4 contaminant.

5 This compound, metam-sodium and its multiple
6 products, are so toxic that to sort of rely on whether it's
7 above this value of MOE or this value of MOE is going back
8 to what Paul said. Questions one's common sense.

9 DR. ALEXEEFF: George Alexeeff with OEHHA.

10 I just wanted to get back to Dr. Fucaloro's
11 earlier question, and actually it's OEHHA that designs the
12 pesticide illness reporting form that's filled out in these
13 cases and then it goes to DPR and to DIR.

14 And we're thinking about trying to improve this
15 reporting form to get more information to help us in this
16 situation.

17 Another responsibility we have is also training
18 physicians on pesticide illness detection and reporting.
19 And one is of course we change the form, we'd have to also
20 train the physicians so they could use it properly. So
21 we're also thinking of doing that. We haven't done much in
22 the area of improving the form or in training physicians in
23 the last several years, but at this point we are planning on
24 doing so or actually we started this year.

25 So it's also the other thing we found, for

1 example, in the metam-sodium incident where we did go to the
2 field and trained the physicians at that point on detecting
3 it and trying to report as much information as possible so
4 we can do retrospective analyses, it's just a hard thing to
5 do in terms of the exposure concentration for getting those
6 samplers there. That's pretty much the hardest thing is to
7 get the exposure information.

8 DR. FUCALORO: I was thinking you'd have certainly
9 a large uncertainty in exposure, but of course you could get
10 the information about when it was applied and you have some
11 historical understanding of what the concentration does as a
12 function of timing and distance from point of application.
13 I mean, I don't know that that's true. I hate to say it's
14 fortuitous when someone gets sick from one of these things,
15 but as Hanspeter was pointing out, you have so little
16 information on human subjects that this is a rare
17 opportunity.

18 DR. KENNEDY: I think your comments about
19 professional education for physicians are fascinating. It's
20 never ending in my particular practice. Our primary
21 inhalent is cordite.

22 CHAIRMAN FROINES: I think that this raises a very
23 important question, Elinor, that we may want to come back to
24 at some point, which is the one thing it's true about
25 pesticides, which we all agree, is that they're toxic. You

1 then debate whether they should be toxic air contaminants.

2 But what we don't have is an -- and we know that
3 pesticides drift, people have occupational exposure and so
4 on and so forth, we need to develop a good surveillance
5 system for addressing pesticide-related health effects.

6 There is no good surveillance system except for
7 what you have in terms of your pesticide injury reports, but
8 the question is is there a way to improve upon that so we
9 can actually develop more information, because you don't
10 have the kinds of interventions that occur in industrial
11 America out there in the field. It's a different ballgame.

12 DR. BLANC: Okay.

13 DR. RUBIN: Okay.

14 CHAIRMAN FROINES: Peter's point is really
15 important.

16 DR. RUBIN: Just to wrap up of some of the things
17 we've talked about.

18 MITC exposure was associated with both short- and
19 long-term effects following the Cantara Loop spill. That we
20 talked about in detail back in November.

21 The acute MOEs for ambient exposure range from,
22 and these are mean values, range from 25 to 2,750. The
23 off-sites from less than one to ten. By our conventional
24 way of thinking, anyway, those off-site MOEs would trigger
25 health concerns because they're based on human data and

1 they're less than ten and even less than one.

2 Subchronic MOEs, again, the ambient from 189 to
3 17,000, the off-site from 2 to 236. The convention is that
4 when based on animal studies an MOE less than a hundred
5 trips a concern.

6 The acute REL value, this is for children and
7 adults, is 22 ppb.

8 The range of acute exposures for ambient is less
9 than 22 ppb, but if the off-site exposures can be way more
10 than 22 ppb, that would indicate again health concerns.

11 Subchronic REL value of 1.5 ppb for the ambient
12 range of exposure from .13 to 4.09, so that value the REL
13 falls right in the middle of that range.

14 The off-site values are quite far above that REL
15 value. That would indicate perhaps some concern.

16 We also discussed in great length the oncogenicity
17 study, and I think we probably agree that some change in
18 language from the original draft that you have is in order.

19 And that's all I have today.

20 CHAIRMAN FROINES: That's very good. Very good.
21 Thank you very much.

22 DR. WITSCHI: I would like to really say it's been
23 pleasant to work with Andrew Rubin on this document and I
24 would like to in the name of the panel thank you very much
25 for the really big big effort you put into that.

1 DR. RUBIN: Thank you.

2 DR. BLANC: Here here.

3 DR. RUBIN: I have the feeling we have not heard
4 the last from MITC, though.

5 CHAIRMAN FROINES: I had one question for OEHHA,
6 George.

7 OEHHA also had comments that were submitted. Do
8 you want to follow up and make any subsequent comments to
9 Andy's remarks?

10 DR. ALEXEEFF: Yes.

11 CHAIRMAN FROINES: Paul and George --

12 DR. ALEXEEFF: We have somebody from OEHHA that
13 can speak to it.

14 CHAIRMAN FROINES: Just one comment, due to the
15 high-level policy operatives, in the future, if we could, it
16 would be nice if we could have integration of your points of
17 view, so we don't see this as an agency war, but rather as a
18 collaborative effort. If that's possible. I'm joking
19 obviously, but --

20 DR. ALEXEEFF: We're not really warring at all.

21 CHAIRMAN FROINES: The point is that we would like
22 to see -- as you bring us comments, we like to see the OEHHA
23 comments, but to the degree they can end up looking similar,
24 because you've come to some common agreement, it's better
25 from our standpoint.

1 DR. WITSCHI: What about the public comments? We
2 talked about that one.

3 CHAIRMAN FROINES: We don't have any public
4 comments.

5 DR. WITSCHI: Yes.

6 DR. KENNEDY: Request for delay.

7 DR. WITSCHI: I would ask Paul that one. When we
8 reviewed the OEHHA documents in the halcyon days, which are
9 past, whenever the SRP or even the lead person got the
10 finished document he also got what many of us considered the
11 most important volumes, these were the public comments,
12 because the public comments sometimes alert you to things
13 you wouldn't spot yourself.

14 I do not recall having seen a document in this
15 case of the MITC, which might have alerted by comments made
16 by interested parties to give a few things a closer look,
17 studies or whatever it was.

18 So my question really is it possible, is it not in
19 your process, that the time being the combined document just
20 OEHHA and from you department and also at this time we get
21 what usually be Part C, the public comments.

22 Because as Stan pointed out if you can get one of
23 those documents, first thing you do is you look at what
24 other people have to say to get your own thinking into gear.

25 MR. GOSSELIN: Yeah. We agree. And I think one

1 of the things, and actually staff has got together
2 yesterday, ARB, OEHHA and DPR, to kind of go over what we
3 have on the plate and we tried to scheduled out in a far
4 better way so we get the ARB, OEHHA consultation done
5 earlier on, the public comment period and public comments
6 and then our response to those is one package, so when you
7 get it it's not a piecemeal event so this thing can go a
8 little smoother.

9 DR. WITSCHI: Yes. I really would like to
10 emphasize that. I would like to see the public comments.

11 MR. GOSSELIN: I agree. It should be, as you
12 said, part of the document with our sort of response or
13 acceptance or rebuttal of that, so it's all there for
14 everyone to see.

15 DR. FUCALORO: We just received one comment that
16 was copied us by a group called the Metam-Sodium Task Force.
17 Did you see that?

18 DR. WITSCHI: I saw that.

19 DR. FUCALORO: That's the only thing I received.

20 DR. WITSCHI: The way I understand the process,
21 the DPR document has to be open for public comments for a
22 certain period of time and people write and I would like to
23 see those letters.

24 DR. FUCALORO: And the practice here that I've
25 understood, and I see what you're getting at, was that there

1 would be a response from OEHHA to the public comments. For
2 example, this document received from Metam-Sodium Task
3 Force, some response to what they say. It's probably a
4 group of three or four chemical companies that obviously
5 have an interest.

6 CHAIRMAN FROINES: But there is one point that is
7 very very important and I guess Stan is probably going to
8 say it. Go ahead. If you don't say it, I will.

9 DR. GLANTZ: You can say it, whatever it is.

10 Well, no, I'll say what I was going to say and
11 then you --

12 DR. FUCALORO: You go, Alphonse. No, Gaston.

13 DR. GLANTZ: But anyway, we have no sense of humor
14 here.

15 I had a couple things.

16 On the point about the OEHHA comments and getting
17 DPR and OEHHA together, I mean, I think, again, we don't
18 want to have an adversarial relationship.

19 And I also want to second what the other people
20 said. I think we've really come a long way in what DPR has
21 been doing vis-a-vis this panel.

22 But I think I wouldn't want to like inhibit
23 OEHHA's comments on the draft, but I think the best --
24 because I think it's helpful, but I think the way it would
25 be nice to handle that is sort of this with the public

1 comments, so that we would get something like the old Part C
2 document.

3 The other thing with regard to this Metam-Sodium
4 Task Force letter, I don't know if this is what you thought
5 I was going to say, I get real irritated with things like
6 this. There is a process and there was public comments on
7 this document sometime in the infinite past. And I think
8 that it's not appropriate for these agencies to send stuff
9 directly to us. It should go to DPR or OEHHA, as
10 appropriate, and then be factored into the public comment
11 process, you know, rather than having people come in at the
12 last second and throwing stuff in front of this panel. This
13 happens from time to time.

14 CHAIRMAN FROINES: But some time ago, years and
15 years ago --

16 DR. GLANTZ: Is that what I was supposed to say?

17 CHAIRMAN FROINES: Yeah.

18 The panel established very clear guidelines about
19 when something would go to the panel. And I don't remember
20 the dates, Bill Lockett may, but it was something like if
21 somebody is going to submit something and they want the
22 panel to review it, it must be at least two weeks before the
23 SRP meeting, and it may have been even longer than that.

24 Do you remember?

25 MR. LOCKETT: Not the exact time, but this was

1 done back in the mid '80s.

2 CHAIRMAN FROINES: Yeah.

3 We set up guidelines and Tom Mack and I sat down
4 and wrote these way back when, and the idea was that we
5 would love to see all the comments that people have to
6 provide us, but it must be within a reasonable time frame so
7 the panel can read it, consider it and then take it up at
8 the meeting.

9 So I would argue that we should -- nothing should
10 be sent to us closer than at least two weeks before the
11 meeting, and if they get it within two weeks -- and because
12 then we were getting Federal Express packages the night
13 before the meeting, which is really insulting.

14 So whatever the date may be, whatever the date the
15 panel wants to have, it seems to me we want to have a window
16 of time between the time we receive a document and the time
17 we consider it at a meeting.

18 And I think otherwise anybody gets to us after
19 that, we don't take it up, period.

20 DR. GLANTZ: And the other thing I recall is that
21 stuff shouldn't be sent by these people to us. It should go
22 to the agency and then come to us through the appropriate
23 channels.

24 And, I mean, I don't -- we didn't do that to be
25 bureaucratic, we did it to be fair and have some control

1 over the process and not get sandbagged.

2 And but, yeah, that's a related point.

3 But I think that the point about bringing -- I
4 mean, I think we did have public comment on the MITC
5 document, it's just this has been going on a long time. And
6 I think that as things speed up, I just think part of the,
7 you know, when you were talking earlier about batching
8 chemicals and things like that, and I think as part of the
9 process you want to have a Part C document.

10 I think that the OEHHA comments on the draft could
11 be handled along with the public comments. And in fact I
12 think in one or two of the things we've seen that's how you
13 did it and I thought that was completely appropriate.

14 Because, again, the way I use these like everyone
15 else is I read the executive summary to kind of figure out
16 what's going on, and then I read the public comments to see
17 what issues are being raised, and then go read the document
18 itself.

19 So anyway, but I think this other thing in this
20 last-minute letter, that's just not appropriate.

21 CHAIRMAN FROINES: Can I stop?

22 I think Stan's finished.

23 But I want to stop because I think Paul has to
24 leave in the next 10, 15 minutes.

25 DR. BLANC: Yes.

1 CHAIRMAN FROINES: Before OEHHA makes any
2 comments, what I'd like to do is get Paul's comments before
3 he has to leave.

4 DR. BLANC: Well, in general what I think I would
5 say is that although the documents as prepared by the DPR
6 may not have everything in exactly the form that we would
7 want in the best of all possible worlds, and there may be
8 some areas of discussion that could be clarified or
9 expanded, this is not a doctoral dissertation and we're not
10 the doctoral review committee.

11 I think the way I would recommend as a matter of
12 process the way we handle clarifications and issues of
13 emphasis would be in our written findings.

14 I think the scientific record is sufficient in the
15 material that we've been provided to make reasonable
16 comments on the indications for metam-sodium and its
17 breakdown products to be treated as toxic air contaminants,
18 and that's what we're required to do.

19 And I would say that we approach it that way
20 rather than trying to seek further editorial modifications
21 in the document.

22 I don't think that there's any question that the
23 fundamental information as provided would support its
24 designation as a TAC, and I think that we simply can serve
25 to better clarify the record by emphasizing the key points

1 as we see them.

2 For example, the pesticides surveillance data
3 that's in the document, for example, and data that is
4 present in the document on the breakdown products and the
5 distribution and the assumptions in the modeling, which are
6 essentially conservative, and for every assumption where you
7 can argue that it could go one way, it could as easily go
8 the other way. So either way you would cut it you would
9 still be saying that it certainly reaches a red flag level
10 consistent with policy for TAC designation.

11 So that's how I would pragmatically approach the
12 problem.

13 DR. GLANTZ: Are you saying, just to be clear, you
14 think the report is okay?

15 DR. BLANC: I think we can come to the conclusions
16 we need to come to based on this report.

17 DR. GLANTZ: So you don't think there's any
18 additional changes they need to make to the document itself?

19 DR. BLANC: I don't think that that's required. I
20 think that we can handle the gaps that we have based on
21 clarifications that we can make in our finding. We can't
22 make a finding based on something that's not even alluded to
23 here. I suppose, although it's possible, that we could
24 comment on the fact that what Paul was alluding to about
25 Kern County having to ban it in the notes, but even that I

1 don't know that that's so germane that we'd be forced to do
2 that.

3 So I recommend that we just move forward.

4 CHAIRMAN FROINES: And Andy has some changes he
5 wants to make.

6 MR. GOSSELIN: Yeah. Actually Tom was going to
7 come up and kind of go over some of the exposure numbers he
8 was looking at in the newer study that will just be an
9 addition to the report and maybe another look at some of the
10 subchronic.

11 DR. BLANC: I don't think we need to meet and
12 review your document again. If you want to give us your
13 final report in the next three weeks or something, in the
14 meantime we could draft our findings.

15 MR. GOSSELIN: And we've done that, I think, in
16 the past on a couple and make sure the numbers that are in
17 there match up with additional data and everything else.

18 CHAIRMAN FROINES: Yeah. And that would mean that
19 we would be basically voting on the document.

20 DR. BLANC: Pending the stated revisions.

21 CHAIRMAN FROINES: Pending the stated revisions.

22 DR. BLANC: Minor revisions.

23 That would be my --

24 DR. WITSCHI: I would agree. I would second that
25 one.

1 DR. GLANTZ: Then why don't you make a motion.

2 DR. BLANC: I move --

3 DR. FRIEDMAN: Can I just ask, is that setting a
4 precedent? Haven't we always been really careful about
5 approving every other document to the last detail before we
6 come up with findings?

7 CHAIRMAN FROINES: No. The DEF document went
8 through an enormous number of changes to bring consistency
9 to the numbers and small errors.

10 DR. GLANTZ: We've never --

11 CHAIRMAN FROINES: We've never -- we have always
12 made small changes that weren't fundamental changes. In
13 fact, the closest thing to actually letting OEHHA or DPR or
14 ARB go was DEF where we actually argued right at the end
15 about NOAEL versus NOEL, and God forbid we ever go back to
16 that argument.

17 And there were some major number errors between
18 OEHHA's numbers and DPR's numbers and so I worked with, I
19 forget who, but we worked it all out to make those changes.

20 But by and large we've generally accepted small
21 changes without necessarily going back.

22 DR. BLANC: I make a two-part motion.

23 CHAIRMAN FROINES: But we could. Whatever you
24 want.

25 DR. FRIEDMAN: I just wanted to raise that

1 question, because this sounded sort of new to me, even
2 though we've always been so careful.

3 DR. GLANTZ: I think what we're talking -- I agree
4 that we've always been very careful, but I think at this
5 point we're talking about small changes to bring consistency
6 within the report, based on the discussion at the meeting
7 and correct some errors that have been identified. I don't
8 think it's anything fundamental.

9 CHAIRMAN FROINES: I think we'll actually -- I
10 think Paul can make a motion and we can second and vote and
11 if something comes up as we discuss it for the rest of the
12 day we can go back and revisit that motion. It's not cast
13 in stone.

14 MR. GOSSELIN: I will say there is the -- I think
15 one of the subjects of the letter you got in about the study
16 in December that we are going to incorporate in the
17 document, that Tom is going to talk about, some new
18 information.

19 CHAIRMAN FROINES: Why don't Paul make the motion
20 and we can go and then if we want to reconsider we can do
21 that.

22 DR. BLANC: Move that the Scientific Review Panel
23 accept the draft document for -- accept the draft document
24 pending minor revisions.

25 DR. WITSCHI: I second.

1 DR. GLANTZ: Can I have one point of
2 clarification? The final acceptance of the document on
3 behalf of the panel would be the chair --

4 DR. BLANC: I want to make a second motion, so let
5 me do that.

6 DR. GLANTZ: Make your second motion.

7 DR. BLANC: First, let's do this one. You have to
8 do one at a time.

9 DR. KENNEDY: Call the vote.

10 DR. GLANTZ: Call the question.

11 CHAIRMAN FROINES: There's no further discussion,
12 then all in favor of that motion.

13 (Show of hands.)

14 DR. GLANTZ: It's unanimous.

15 DR. BLANC: My second motion is that the chair of
16 the panel review the revisions and in light of the draft and
17 its revisions, draft findings for the panel to be circulated
18 to its members.

19 CHAIRMAN FROINES: Well, I would, if I can add to
20 that, I would say if the review indicates significant
21 changes --

22 DR. BLANC: Certainly.

23 CHAIRMAN FROINES: -- then I would bring it back
24 to the panel for --

25 DR. BLANC: Fine.

1 CHAIRMAN FROINES: -- reconsideration.

2 DR. BLANC: I accept your friendly amendment.

3 So let me read it to you so you have it, or state
4 it to you.

5 The chair will review the revised draft
6 document --

7 CHAIRMAN FROINES: I have a second friendly
8 amendment. Sorry. Sorry.

9 I'm concerned about meeting Gary's question. I
10 think it's important.

11 That the chair and the lead person --

12 DR. BLANC: Who is the lead person?

13 CHAIRMAN FROINES: Peter.

14 DR. BLANC: So that resolve then the chair and the
15 lead reviewer will evaluate the revised document and either
16 request further review by the whole panel or draft findings
17 to be circulated for review by the panel.

18 DR. KENNEDY: Second.

19 DR. WITSCHI: Thank you.

20 CHAIRMAN FROINES: I just don't want anybody to
21 say --

22 DR. GLANTZ: Just a point of clarification,
23 though. I mean, I think it's clear if there's any
24 substantive changes to the document, then it would come back
25 to the panel.

1 CHAIRMAN FROINES: Absolutely.

2 DR. GLANTZ: That the review by the chair is to
3 simply make sure that any changes that are made are
4 consistent with the views expressed by the panel.

5 DR. FUCALORO: I understood it that way.

6 DR. GLANTZ: Just for the record.
7 Call the question.

8 CHAIRMAN FROINES: All in favor.

9 (Show of hands.)

10 DR. GLANTZ: It's unanimous for the record.
11 You're supposed to say that.

12 DR. FUCALORO: Since he never does, you always do.

13 DR. GLANTZ: I know. It's because I am so
14 meticulous.

15 CHAIRMAN FROINES: It's always so much fun when
16 you add in your little pieces and everybody enjoys it, so
17 why would I take that away?

18 Okay. Can we take a five-minute break? I mean a
19 five-minute break. We can finish with this fairly quickly.

20 DR. GLANTZ: We don't have draft findings already,
21 do you?

22 CHAIRMAN FROINES: No. I wish we did.

23 Five-minute break and we're going to hear from
24 OEHHA and then the other.

25 MR. GOSSELIN: We have a short presentation that's

1 going to be changes to the document and then OEHHA.

2 (Thereupon a short recess was taken.)

3 MR. GOSSELIN: We have ten-minute presentation, or
4 shorter than that, and then OEHHA is going to wrap up. This
5 is just on the exposure monitoring and one new study that
6 came in that's going to be added to the document.

7 If we can go right to the overheads.

8 CHAIRMAN FROINES: Yeah. I have a question. How
9 long is OEHHA -- does OEHHA want to make any presentation
10 and, if so, how long would it take?

11 DR. ALEXEEFF: Two minutes.

12 CHAIRMAN FROINES: Two minutes.

13 You're considering how long?

14 DR. THONGSINTHUSAK: Ten minutes.

15 CHAIRMAN FROINES: Ten minutes. That's 12
16 minutes. I'm only asking because Peter just said that
17 there's some panel members who can make a 3:45 plane if we
18 finish in time.

19 DR. FUCALORO: Make that 3:40. I have to get a
20 car back to the rental.

21 CHAIRMAN FROINES: If we were to move in that
22 direction, we haven't had a discussion -- the trouble with
23 Paul making his motion is that we have nobody on the panel
24 has had a chance to give comments to DPR on their reading of
25 the document. So I think --

1 DR. GLANTZ: Our reading of which document?

2 MR. GOSSELIN: Which document?

3 CHAIRMAN FROINES: The documents.

4 DR. GLANTZ: I thought we were --

5 DR. BYUS: We just voted for it.

6 CHAIRMAN FROINES: I'm still saying that we did
7 vote for it, but nobody has had an opportunity, besides
8 Paul, we have had a lot of discussion, enormous discussion
9 during the day, so the question is are there any members of
10 the panel who still would like to raise questions with DPR,
11 so that they get their positions stated?

12 And, if not, we'll go with the -- try to make the
13 airplanes. I don't mean to create a Hobson's choice.

14 DR. GLANTZ: I thought that's what we spent the
15 whole morning doing.

16 CHAIRMAN FROINES: Your plane or your freedom.

17 DR. GLANTZ: I thought, John, that's what we spent
18 half the morning doing.

19 CHAIRMAN FROINES: Okay. I'm just --

20 DR. GLANTZ: I don't want to shut anybody else
21 down, but I thought --

22 DR. FUCALORO: Shut us down.

23 CHAIRMAN FROINES: All I'm --

24 DR. GLANTZ: Don't say things like that on the
25 record. We're all going to be arrested and sued.

1 CHAIRMAN FROINES: Stan, you don't get it. He may
2 have said it, nobody would have noticed. You just
3 reinforced it.

4 DR. GLANTZ: And you just reinforced me. It's
5 been a long meeting.

6 CHAIRMAN FROINES: Okay. A very good meeting.

7 DR. GLANTZ: It has been a very good meeting.

8 CHAIRMAN FROINES: As long as everybody feels fine
9 about this process of doing -- excuse me, let me finish my
10 talking.

11 We will go to a final presentation by DPR, a short
12 presentation by OEHHA, and then we will essentially adjourn,
13 unless somebody asks for a reconsideration and wants to have
14 more comments.

15 Is that acceptable?

16 DR. GLANTZ: Can I just say one thing to clarify
17 the record?

18 I would say the question you should have asked is,
19 Mr. Chairman, does anyone have any additional comments about
20 the document.

21 CHAIRMAN FROINES: Okay.

22 DR. GLANTZ: To guide DPR beyond what we've
23 already discussed so far in the meeting.

24 CHAIRMAN FROINES: Tony?

25 DR. FUCALORO: No.

1 CHAIRMAN FROINES: Peter?

2 I think he's already voting with his head.

3 Roger said no.

4 Craig, I think, is saying no. He's trying to
5 reach his coffee.

6 So let's go ahead.

7 DR. THONGSINTHUSAK: I'm Tom Thongsinthusak.

8 I would like to present the data from the letter
9 submission from the Metam-Sodium Task Force. It's an
10 off-site and monitoring studies conducted in 1999. The area
11 is in Bakersfield, California.

12 Table 1, summary of the air concentrations of MITC
13 from the application of metam-sodium through sprinkle
14 irrigation. I present the table in two sections. The
15 middle section is for ADD. This is for short-term exposure.
16 And the last part is on the right-hand for SADD or seasonal
17 daily doses. This is for subchronic exposure.

18 For this study, there were four to five sampling
19 stations located 150, 300, 700 and 9700 meters, in the east
20 and the west areas of the treated field.

21 This treated field consists of about four plots of
22 20 acres each.

23 And the maximum application of metam-sodium was
24 applied, and the application was in accordance with the
25 technical information bulletin. In other words, the

1 procedure in the application including pre-application
2 irrigation and after the application it was a water tap to
3 retain metam-sodium or MITC.

4 I group them into day one, day two, day three and
5 day four for short-term exposure. Start on day one for the
6 highest, down the road and then for the subchronic, the
7 average of the four-day concentration, so they can be used
8 for the subchronic exposure estimates.

9 Next, please.

10 The second table is similar to the first one, but
11 this is the metam-sodium was applied through shank
12 injection. The total area is about 79 acres of land.

13 Also there were four sampling stations located in
14 the east and the west of the field. Also, air
15 concentrations include four different days. That's for ADD
16 and SADD.

17 CHAIRMAN FROINES: How do we know -- I'm sorry, I
18 missed something. How do we know what the wind patterns
19 were for these determinations?

20 DR. THONGSINTHUSAK: Yes, I will show them on the
21 next table.

22 CHAIRMAN FROINES: Okay.

23 DR. THONGSINTHUSAK: This is summary, and the
24 study assume that the sampling station was in the downwind
25 areas, but according to the data I revealed it's not exactly

1 the way they wanted to see. Like this stand 150, 300 and
2 700 sampling stations A, C and A. Let's suppose that A,
3 station A, should be in downwind direction, but because of
4 the wind shifted, the C showed the highest air concentration
5 in that direction.

6 So for the short-term exposure I pick the highest
7 air concentration, I mean the daily air concentration, to
8 represent the daily exposure for acute risk assessment.

9 And for the SADD, the sampling station is pretty
10 consistent, when I take the average of the four sampling
11 days, the high always in the A sampling station for 150, 300
12 and 700 meter stations.

13 For the acute exposure at 150 meters from the
14 treated field, the air concentration is 101 parts per
15 million. For the 300 it's 52. 700 meters it is 31.

16 And air concentration daily dosage represents ADD
17 in term of micrograms per kilogram and per day. I would not
18 repeat those numbers.

19 For the SADD or the subchronic exposure, the mean
20 I showed the air concentrations as mean, low and high for
21 all three sampling stations.

22 For example at 150 meters, mean value for the air
23 concentration is 55 parts per billion.

24 And for the low, 50, and the high 63, and so on
25 and so forth.

1 And then I calculate the subchronic exposure in
2 terms of SADD. This is for adult female exposures.

3 For the 150 represents 100, for 486 the low is 5.5
4 and the high 6.9.

5 Next, please.

6 DR. FRIEDMAN: Can you explain why it's lower for
7 SADD than ADD?

8 DR. THONGSINTHUSAK: Because I take the average of
9 those four daily exposures. The first day will be higher
10 than most of the time, the second day, third day and so on
11 and so forth.

12 DR. FRIEDMAN: So this is one -- there is an
13 application --

14 DR. THONGSINTHUSAK: Yes.

15 DR. FRIEDMAN: And then the A is right after the
16 application and then it gradually disperses?

17 DR. THONGSINTHUSAK: That's right. That's
18 correct.

19 The format is similar to Table 3 on the previous
20 table, but this is for the shank injection method.

21 Presentation of the data is the same. The mean
22 for a short-term exposure and the moderate-term exposure at
23 150, 300, and 486 meter sampling stations.

24 I would cite one example for the ADD run from 175
25 parts per billion for sampling at 150; for 300, 106; and 486

1 meters, 84 parts per billion.

2 Overall for two different methods, I mean
3 sprinkler injection and shank injection, the air
4 concentrations at similar distance from the treated field
5 were similar.

6 And in my previous presentation, probably in
7 November, there's a question about a retention of the silica
8 gel tubes. This study has or used similar methods to that
9 one. The previous one was conducted by ICI, and they use a
10 silica gel dry tube, but they did not add residues of MITC
11 from the tube to the total MITC residues.

12 I did not have any good answer for that. But this
13 study can replace the previous one and the air
14 concentrations at the same distance from the treated field
15 was very similar.

16 So I propose that this study be used to replace
17 the previous one, which was conducted by ICI, and there was
18 so many questions about a retention of silica gel drying
19 tubes, and the study did not include the residue in those
20 tubes.

21 DR. FUCALORO: Are the results of this study
22 significantly different from the one, the one that was in
23 question? I don't remember.

24 DR. THONGSINTHUSAK: Very similar.

25 DR. FUCALORO: Very similar?

1 DR. THONGSINTHUSAK: Yes.

2 DR. FUCALORO: Okay.

3 DR. THONGSINTHUSAK: But we still have some work
4 to do for this study, because the downwind direction did not
5 stay put in the same direction all the time, and some MITC
6 residues at relatively high amount was observed in the
7 upwind area.

8 So I assume there was the wind shift, the
9 direction did not go to the same direction during that four
10 days of study.

11 Since the letter representative the metam-sodium
12 application methods that currently used in California, I
13 assume that in general the study should be more
14 representative than the previous study.

15 CHAIRMAN FROINES: Where was this study conducted?

16 DR. THONGSINTHUSAK: Pardon me?

17 CHAIRMAN FROINES: Where was it conducted?

18 DR. THONGSINTHUSAK: Where was it conducted? In
19 Bakersfield.

20 CHAIRMAN FROINES: Bakersfield.

21 DR. THONGSINTHUSAK: Yes. In 1999.

22 This is the last slide.

23 CHAIRMAN FROINES: How do we know about how much
24 metam-sodium was actually used relative to other studies
25 that have been conducted?

1 MR. GOSSELIN: You mean the rates of application?
2 That should be part of the whole study report is to -- the
3 method, injection depth or the sprinkler or how long it took
4 to put the application on and how much material was actually
5 put out.

6 And to kind of put that study and these other
7 studies into context, all those variables, including the
8 specific weather data and the residues that were found and
9 everything else were used by staff in a similar way that
10 Melanie described to us taking and doing some modeling to
11 calculate out on either a regional, statewide basis what the
12 air levels would be and make sure that we don't exceed an
13 REL.

14 CHAIRMAN FROINES: Exceed an REL as opposed to
15 MOE?

16 MR. GOSSELIN: Depends on --

17 CHAIRMAN FROINES: All this continues to reinforce
18 this problem and that is that exposures are highly variable.

19 MR. GOSSELIN: Right.

20 CHAIRMAN FROINES: And defining decision criteria
21 on highly variable parameters is a problem.

22 DR. THONGSINTHUSAK: This is the last overhead.

23 The last time I did not show chronic exposure
24 estimates, and this one I estimated chronic exposure from
25 three ambient air monitoring studies. The first one

1 conducted in Kern County and the second Bakersfield by
2 Seiber and his colleague.

3 And number of potential exposure days, which is at
4 the bottom as a footnote, it was estimated to be 188 days
5 per year and the range is 79 to 328 days.

6 So I only estimated the exposure for these three
7 because the ambient air concentrations should be more
8 representative than the application site and monitoring
9 study.

10 In the last column I represent annual exposure
11 SADD, annual average daily dosage.

12 For example at a Shafter site the range is .001 to
13 .32 and the median is .05. For B7, Bakersfield, Lamont, in
14 the houses it showed AADD is .32, the range from .02 to
15 1.76, so on and so forth.

16 CHAIRMAN FROINES: I have a question. I don't
17 want to hold it up.

18 Why do you have parts per million on one side and
19 ADD in micrograms per kilogram on the other?

20 DR. THONGSINTHUSAK: The ppb represent the
21 airborne concentrations of MITC. The AADD represents the
22 absorbed dose.

23 So the risk assessor can use either values.

24 CHAIRMAN FROINES: The reader will generally find
25 things in similar units to be better, if you can do it.

1 DR. GLANTZ: It's fine. Depends on what you're
2 trying to do with it.

3 CHAIRMAN FROINES: Okay.

4 DR. THONGSINTHUSAK: That's all I have, unless you
5 have questions.

6 It's been a little bit over ten minutes.

7 CHAIRMAN FROINES: That's all right.

8 DR. KENNEDY: Thank you.

9 DR. WITSCHI: What was the difference between
10 those data and what you showed earlier, summer 1997 to
11 winter 1998?

12 DR. THONGSINTHUSAK: Sorry?

13 DR. WITSCHI: In an earlier slide, very similar
14 data for Lamont and Shafter and Seiber identified those Kern
15 County in summer 1997 for Kern County winter 1998. Is this
16 the same study or is this a different study?

17 DR. THONGSINTHUSAK: The same study.

18 DR. WITSCHI: Same study.

19 DR. THONGSINTHUSAK: It's the ambient air
20 monitoring study.

21 DR. WITSCHI: Same study?

22 DR. THONGSINTHUSAK: Yeah. from Lamont.

23 DR. WITSCHI: The numbers are not the same.

24 DR. THONGSINTHUSAK: The second one by Seiber,
25 that's a different one.

1 DR. GLANTZ: I think rather than replacing what's
2 in the report with this study, you should just add it.

3 MR. GOSSELIN: That's what we're going to do.

4 DR. THONGSINTHUSAK: That's right.

5 DR. GLANTZ: That's a suggestion.

6 DR. FUCALORO: The explanation.

7 DR. GLANTZ: Just add it. Don't take what you've
8 got in there out.

9 DR. THONGSINTHUSAK: Yes.

10 DR. FUCALORO: Validate the other.

11 DR. GLANTZ: Yeah. It's the results are so
12 similar, it actually tends to affirm it.

13 DR. THONGSINTHUSAK: Okay. Thank you.

14 CHAIRMAN FROINES: Further comments?
15 George.

16 DR. ALEXEEFF: George Alexeeff with OEHHA.

17 I just want to say right off the bat our findings
18 are very consistent with the report, with the DPR report.

19 And we've actually worked very closely with this
20 one, and the major difficulty we had was just keeping up
21 with their revised versions of it and it's something that
22 we're working on to actually improve that so that sometimes
23 our findings are not -- are in sync with the current version
24 that they have as opposed to an older version.

25 But that's pretty much the biggest difference, the

1 difficulty we had.

2 We will revise our finding on oncogenicity so it's
3 consistent with what the panel discussed here today, and
4 it's more similar to what their older version or their
5 current document says.

6 The other thing is that we did a little bit
7 differently is emphasized a couple things differently in
8 here, concerns that we had about uncertainties.

9 One was the concern about RADS, reactive airway
10 dysfunction syndrome. We kind of emphasized that, that
11 we're concerned about that as an outcome of an extensive
12 exposure.

13 The other one is, and you talked --

14 DR. KENNEDY: In what regard?

15 DR. ALEXEEFF: In that spill that occurred of
16 metam-sodium in the Cantara Loop, we think that it would be
17 very likely to -- the health department, we did a study with
18 the health department, Department of Health Services, excuse
19 me, and we think that many of the individuals, about 20 or
20 so, developed reactive airway dysfunction syndrome, as a
21 result of the exposure, which I think is one of the first
22 times an environmental exposure has resulted in that
23 syndrome.

24 DR. KENNEDY: Sensitization syndrome?

25 DR. ALEXEEFF: Yeah.

1 So we think that's something that was important to
2 us and it could be the MITC, it could be the MIC. We don't
3 know. But we thought it was an important finding.

4 DR. KENNEDY: Has there been any -- is there an
5 ongoing long-term follow-up with those patients for scar
6 cancers?

7 DR. ALEXEEFF: I don't know. I can ask the lead
8 physician.

9 DR. KENNEDY: Interesting to do over, say, 15
10 years.

11 DR. ALEXEEFF: Dr. Jim Cohn was the lead on that
12 and he's with Department of Health Services.

13 CHAIRMAN FROINES: George, I don't see in here
14 something about discussion of RADS.

15 DR. ALEXEEFF: Yeah, it's in there.

16 CHAIRMAN FROINES: Where?

17 DR. ALEXEEFF: It is in our findings. It's
18 actually the last findings, I think, that mentions it and
19 then the last word of our findings is RADs.

20 CHAIRMAN FROINES: I saw that.

21 DR. ALEXEEFF: And there's another finding.

22 CHAIRMAN FROINES: Where is it?

23 DR. ALEXEEFF: Finding No. 10. Our finding No.
24 10.

25 So this was simply a measure of emphasis, and then

1 also although we agreed with their choice for that human
2 exposure study, you know, when you look at the -- weigh
3 everything together, we also just felt it was important to
4 look at the pros and cons of the animal study and the human
5 study, because we sort of felt that neither of them are
6 exactly what we'd like, so we kind of made a big deal about
7 that in our findings, but just so that everybody understood
8 the uncertainties of both studies or the pros and cons.

9 CHAIRMAN FROINES: There's no harm in using
10 developing numbers from both studies. It doesn't have to be
11 a bright line. It can say there are problems with this
12 study, but this gives us these results, there's a problem
13 with this study, this gives us these results and then you
14 have covered your bases.

15 DR. ALEXEEFF: Yeah.

16 And I guess the last point, and this is not really
17 directly related to the findings, but in response to
18 Dr. Rubin's comments on how to address the multi-chemical
19 situation, we can talk with their staff regarding the hazard
20 index approach, which is what we are developing in the hot
21 spots guidelines, of course the guidance isn't out yet, but
22 we can explain to them what the approach is, the US EPA
23 based approach is, and to see if that sheds any light.

24 CHAIRMAN FROINES: You say on your finding 24,
25 OEHHA does not include a RAD on human breathing adjustment.

1 DR. ALEXEEFF: Correct.

2 CHAIRMAN FROINES: And you all need to work that
3 out.

4 DR. ALEXEEFF: Yeah.

5 CHAIRMAN FROINES: And come back to us on that.

6 DR. ALEXEEFF: I agree. Paul and I talked about
7 that one earlier today, and that is something we do want to
8 try to work out. It has to do with simply the way staff
9 have done their work in the different departments, and we
10 need to work a couple of those things out.

11 CHAIRMAN FROINES: I want to emphasize one thing
12 quickly. I think the RADS issue is really a major issue.
13 It also goes to the question of chronic disease versus acute
14 disorders. So it's something I think we should try and
15 follow up on, because I think if we can -- if there's an
16 issue of MITC or MIC producing RADS, that's a major health,
17 potentially important health problem.

18 I think that's what Peter was --

19 DR. ALEXEEFF: Okay. That's all.

20 CHAIRMAN FROINES: Well, I was just going to
21 say --

22 DR. KENNEDY: You better say it fast.

23 CHAIRMAN FROINES: Does anybody else on the panel,
24 while you're still within the room, have any further
25 comments?

1 DR. FUCALORO: I need to make a few comments with
2 slides.

3 DR. GLANTZ: I'd like to make a comment that we
4 adjourn.

5 CHAIRMAN FROINES: Move that we adjourn?

6 DR. GLANTZ: I move that we adjourn.

7 DR. ATKINSON: Second.

8 DR. GLANTZ: Call the question.

9 CHAIRMAN FROINES: The question, all in favor, was
10 unanimous.

11 (Thereupon the meeting was adjourned
12 at 2:45 p.m.)

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CERTIFICATE OF SHORTHAND REPORTER

I, JANET H. NICOL, a Certified Shorthand Reporter of the State of California, do hereby certify that I am a disinterested person herein; that I reported the foregoing meeting in shorthand writing; that I thereafter caused my shorthand writing to be transcribed into typewriting.

I further certify that I am not of counsel or attorney for any of the parties to said meeting, or in any way interested in the outcome of said meeting.

IN WITNESS WHEREOF, I have hereunto set my hand this 8th day of February 2000.

Janet H. Nicol
Certified Shorthand Reporter
License Number 9764