

MEETING
STATE OF CALIFORNIA
AIR RESOURCES BOARD
SCIENTIFIC REVIEW PANEL

SOUTH SAN FRANCISCO CONFERENCE CENTER
255 SOUTH AIRPORT BOULEVARD
SAN FRANCISCO, CALIFORNIA

TUESDAY, NOVEMBER 30, 2004

9:00 A.M.

JAMES F. PETERS, CSR, RPR
CERTIFIED SHORTHAND REPORTER
LICENSE NUMBER 10063

PETERS SHORTHAND REPORTING CORPORATION (916) 362-2345

APPEARANCES

PANEL MEMBERS

Dr. John Froines, Chairperson

Dr. Paul Blanc

Dr. Craig Byus

Dr. Stanton Glantz

Dr. Katharine Hammond

Dr. Joseph Landolph

Dr. Charles Plopper

REPRESENTING THE AIR RESOURCES BOARD

Mr. Jim Aguila, Manager, Substance Evaluation Section

Mr. Lynton Baker, ARB, Air Pollution Specialist

Mr. Jim Behrmann, Office of Health Advisor

Mr. Robert Krieger, Air Pollution Specialist

Mr. Peter Mathews, Office of Health Advisor

REPRESENTING THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD
ASSESSMENT:

Dr. George Alexeeff, Deputy Director, Scientific Affairs

Dr. James Collins, OEHHA, Staff Toxicologist

Dr. Melanie Marty, OEHHA, Chief, Air Toxicology and
Epidemiology Section

Dr. Mark Miller, OEHHA

Dr. Andy Salmon, Chief, Air Risk Assessment Unit

Dr. Bruce S. Winder, OEHHA, Associate Toxicologist

REPRESENTING THE DEPARTMENT OF PESTICIDE REGULATION

Ms. Mary-Ann Warmerdam, Director, DPA

PETERS SHORTHAND REPORTING CORPORATION (916) 362-2345

INDEX

PAGE

1.	Continuation of discussion of a toxicity summary and proposed chronic Reference Exposure Level for respirable crystalline silica, an addendum to "Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III: Technical Support Document, Determination of Noncancer Chronic Reference Exposure Levels."	3
2.	Review of the draft report "Proposed Identification of Environmental Tobacco Smoke as a Toxic Air Contaminant," October 2004.	67
3.	Consideration of administrative matters.	61
	Adjournment	212
	Reporter's Certificate	213

PROCEEDINGS

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

CHAIRPERSON FROINES: We can officially open the November 30th, 2004, Scientific Review Panel meeting.

And at the outset I want to make two brief announcements. One is, when traffic permits the new Director of the Department of Pesticide Regulation is going to attend our meeting. And I'm going to introduce her and she's going to make a couple of remarks. So since she's had traffic problems coming down from Sacramento, she's running a little late.

So we'll stop, Melanie, the silica presentation -- presumably she'll be here during the discussion during that -- and give her chance a to say hello to the panel.

So that's very nice gesture on her part to come to this meeting even though we're not taking up a DPR pesticide.

The second announcement is -- and her name, by the way, is Mary-Ann Warmerdam. And so -- but we'll introduce her when she arrives.

The second item is, we now have for the first time in a few years -- and Peter or Jim probably knows how long it's been. But for the first time in a few years we have a complete panel. There are two members of the panel who are not here today, Gary Friedman and Roger Atkinson.

1 But our new member of the panel, who we would like to
2 welcome is Dr. Charles Plopper from the University of
3 California at Davis.

4 And so I think it might be useful if we just went
5 around the room and each person introduce themselves to
6 Charlie and said where you are from.

7 PANEL MEMBER BLANC: Could we just Go around the
8 table? Would that be okay?

9 CHAIRPERSON FROINES: That's what we're doing.

10 PANEL MEMBER BLANC: Instead of the whole room.

11 CHAIRPERSON FROINES: Did I a say the room?

12 (Laughter.)

13 CHAIRPERSON FROINES: No, the room can relax.

14 (Laughter.)

15 CHAIRPERSON FROINES: Joe.

16 PANEL MEMBER LANDOLPH: Charlie knows me. USC.

17 I studied carcinogenesis and mutogenesis. We also went
18 through similar branches of the Army together a long time
19 ago, right? And have sat on review panels together.

20 PANEL MEMBER GLANTZ: I'm Stan Glantz. I'm a
21 Professor of Medicine at UCSF. And I'm in the Cardiology
22 Division and do a lot of work on tobacco.

23 PANEL MEMBER HAMMOND: I'm Kathy Hammond at
24 University of California Berkeley, School of Public
25 Health, Environmental Health Division. And my research is

1 particularly focused on exposure assessment --
2 epidemiologic studies.

3 CHAIRPERSON FROINES: Craig.

4 PANEL MEMBER BYUS: Craig Byus, University of
5 California Riverside, Biomedical Sciences Program, work on
6 cancer-related change expression.

7 PANEL MEMBER BLANC: Paul Blanc, UCSF,
8 Occupational and Environmental Medicine.

9 CHAIRPERSON FROINES: Roger, as you probably
10 know, is an atmospheric chemist. And Gary Friedman is of
11 course our epidemiologist.

12 So that we have a full panel. And I think it's
13 in some respects the best panel we've ever had. Not
14 taking away from any previous incumbents.

15 So the first item on the agenda, unless somebody
16 has something else, is the continuation of the discussion
17 of the toxicity and chronic reference exposure level for
18 respirable crystalline silica.

19 And, Melanie, are you going to make a
20 presentation?

21 (Thereupon an overhead presentation was
22 Presented as follows.)

23 SUPERVISING TOXICOLOGIST MARTY: Yeah, I'll just
24 introduce -- Jim Collins will make the presentation. But
25 just a couple introductory remarks.

1 Today we're going to review the changes made to
2 the chronic reference exposure level in response to the
3 Panel comments.

4 The Panel reviewed and discussed the crystalline
5 silica chronic REL on the May 19th meeting. And there
6 were a number of comments made by the Panel regarding the
7 percent of dust that was crystalline silica in the
8 epidemiologic studies and also the particulate matter
9 fraction to which the REL should apply.

10 So with that I'm just going to hand it over to
11 Jim.

12 DR. COLLINS: Next slide.

13 CHAIRPERSON FROINES: Jim, before you get
14 started.

15 Charlie, just for your information, this chemical
16 has two lead persons that took responsibility for working
17 with the agency to try and ensure the best product as the
18 document comes to the panel. And the lead for silica was
19 Paul Blanc and Kathy Hammond. And in general we have
20 historically always identified lead persons on a
21 particular chemical. So when the -- I'm sorry. I
22 apologize. So when the presentation is finished, Paul and
23 Kathy will be the first two people to comment on the
24 silica document. And then we basically go around the room
25 and hear from each panel member.

1 DR. COLLINS: Okay. I'm Jim Collins. I'm a
2 toxicologist with the Air Section of the OEHHA.

3 The silica chronic REL was discussed at the may
4 19th meeting. We used a standard benchmark concentration
5 with USEPA BMDS software. We used a well conducted
6 epidemiology study of white gold miners in South Africa
7 conducted by Hnizdo and Sluis-Cremer. And our chronic REL
8 is supported by several other studies of silicosis: In
9 South Dakota gold miners by Steenland and Brown; in
10 diatomaceous earth workers by Hughes, Checkoway and
11 others; and Chinese tin miners by Chen, et al., with
12 assistance from NIOSH.

13 Next slide please.

14 --o0o--

15 DR. COLLINS: This study was published in 1993.
16 It consisted of 2,235 white South African gold miners who
17 were exposed in their work place. Three hundred thirteen
18 of the minors had silicosis, that is, a disease of the
19 respiratory system as then ILO classification of 1 over 1,
20 which is definite silicosis.

21 Go to the next slide and we'll come back to this.

22 --o0o--

23 DR. COLLINS: Here is a plot of the incidence
24 data, the dose of the cumulative dust exposure of the
25 miners on the X axis, and on the Y axis is the fraction of

1 the miners affected with silicosis.

2 Go back now.

3 --o0o--

4 DR. COLLINS: From using the probit model with
5 the log dose of the concentration, we obtained a BMC01,
6 that is, the lower bound expected to cause 1 percent
7 incidence of silicosis, 2.1 milligrams per cubic
8 meter-years of cumulative dust exposure, which is
9 equivalent to .636 milligrams per cubic meter-year of
10 silica. That BMC is basically at the same level as the
11 low -- as the NOAEL observed in the study. These miners
12 were exposed eight hours per day roughly, five days a
13 week. We assume they took in half their air concentration
14 while they were working. The average exposure was 24
15 years. The range was from 10 to 39 years.

16 Okay. Next slide.

17 This is the plot. And then the next slide.

18 --o0o--

19 DR. COLLINS: From this 636 microgram per cubic
20 meter-year average exposure, we divided by 24 years, the
21 average time of exposure, and we came up with a number of
22 26.5 micrograms per cubic meter as the average worker
23 exposure. And this is equivalent to a continuous
24 environmental exposure of 8.75 micrograms per cubic meter.

25 We then added several uncertainty factors. We

1 did not need a LOAEL UF because you don't need one in the
2 BMC approach. We did not need a subchronic uncertainty
3 factor because the chronic exposure of 10 -- of 39 years.
4 We did not need an interspecies uncertainty factor because
5 we were looking at humans.

6 We did insert an intraspecies factor of 3 because
7 although a large number of men were studied and some of
8 them would be sensitive, there were no women or children
9 exposed. So we put in an intraspecies uncertainty factor
10 of 3, which means the total uncertainty factor was 3.

11 And the chronic REL, 3 micrograms per cubic meter
12 of respirable crystalline silica.

13 And whereas previously we included that as the
14 PM10 fraction based on panel comments, it's now -- the
15 occupational standard is measured by NIOSH, and the NIOSH
16 method depends on the ACGIH.

17 Next slide please.

18 --o0o--

19 DR. COLLINS: So one of the major comments of the
20 panel was that we should use the respirable silica
21 particle size as defined occupationally. And in response
22 we did that. We changed the document and the proposed REL
23 were changed to reflect that comment.

24 Next slide please.

25 --o0o--

1 DR. COLLINS: The second comment, Dr. Blanc asked
2 us to include additional studies on slate workers in
3 Wales. We did that, Glover, et al., 1980. We also found
4 data on slate pencil workers in India; two references on
5 that. And it was suggested that we remove the study of
6 coal workers because they had very high exposures, and it
7 was at least relevant to the REL.

8 We made those changes. We also added a study of
9 black South African gold mine workers. The blacks
10 actually make up a majority of the workers in the gold
11 mines. That study was published since the last meeting.
12 So we included that study as well as an earlier study
13 doing autopsies of black gold miners.

14 Next slide please.

15 --o0o--

16 DR. COLLINS: There were a variety of Editorial
17 changes and clarifications that were made. And if they
18 were made too tersely, it was probably my fault. If they
19 were made extensively, it was due to Andy's work.

20 Next slide please.

21 --o0o--

22 DR. COLLINS: The final comment that we addressed
23 was that we further investigate the issue about silica
24 content of the dust in the study by Hnizdo and
25 Sluis-Cremer raised in the comments by Gibbs and the

1 American Chemical Council.

2 Next slide.

3 --o0o--

4 DR. COLLINS: Basically the comment is the silica
5 content of acid-washed mine dust is 54 percent, not 30
6 percent.

7 And quoting from Gibbs' -- Du Toit's 2002 paper:

8 "With many uncertainties we estimate that the quartz
9 exposures of South African miners derived from past
10 theoretically based conversions from particle number to
11 respirable mass underestimate the actual quartz exposures
12 by a factor of about 2."

13 Next slide please.

14 --o0o--

15 DR. COLLINS: We reviewed the independent
16 reporting of the underlying data by Page-Shipp and Harris.
17 Page-Shipp and Harris basically published Beadle, who did
18 most of the surveying. After Beadle died, Page-Shipp and
19 Harris went over his work. An analysis by OEHHA staff, in
20 this case Dr. Salmon, indicated that Hnizdo and
21 Sluis-Cremer used the correct silica content of 30
22 percent, despite a confusing, in fact erroneous, statement
23 in footnote to Table 2 of their paper.

24 We sent our analysis to Hnizdo, and she agreed
25 that our analysis was clear to her and she thought she

1 agreed with it.

2 These calculations are now displayed in Table 18
3 of the chronic REL summary.

4 --o0o--

5 DR. COLLINS: Our next step, we need to be sure
6 we've addressed the Panel's comments, respond to any
7 further comments. And then after the panel approval, the
8 OEHHA director will adopt the chronic REL for use in Hot
9 Spots risk assessments.

10 That's the end of our presentation.

11 CHAIRPERSON FROINES: Okay. Thank you.

12 Paul.

13 PANEL MEMBER BLANC: There was a question that I
14 had at the previous meeting which had some bearing on the
15 mathematical calculations. And that's the presumption
16 that even white miners in South Africa in the time period
17 studied would have worked eight-hour shifts only five days
18 a week. Did you --

19 DR. COLLINS: If you go to the -- is it Table 19
20 now? Let me see.

21 Yeah, do we have a -- it's in the text, Table 19.
22 I'm sorry. Table 19 of our revised document shows in -- I
23 don't know if we have an overhead projector.

24 SUPERVISING TOXICOLOGIST MARTY: We do.

25 DR. COLLINS: Oh, okay.

1 It's now Table 19 of the document. If you go to
2 the first line in that, it shows that different people had
3 different shift hours. And so that has been accounted
4 for, we think.

5 PANEL MEMBER BLANC: And that was five days a
6 week? They had two days off in South Africa?

7 DR. COLLINS: As far as we know, based on
8 discussing this with Hnizdo. We showed her our analysis,
9 and she --

10 PANEL MEMBER BLANC: Can you just double check
11 that other question? It sounds like you've gone the extra
12 mile in terms of the hours. But --

13 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
14 SALMON: The claim is it's been normalized to, you know,
15 an eight-hour shift five days a week basis. But we will
16 certainly double check that and make sure that our
17 understanding is correct.

18 PANEL MEMBER BLANC: Aside from that --

19 PANEL MEMBER HAMMOND: I think that that's what
20 Page-Shipp have done in their paper. I think that they
21 actually say they've normalized it, downshift.

22 PANEL MEMBER BLANC: Okay. The terms of the
23 general issue, the what is the correct calculation of the
24 percentage of silica, which has become such a focal point
25 of debate because obviously it would upshift your --

1 DR. COLLINS: -- three to five.

2 PANEL MEMBER BLANC: -- from three to five. I
3 found your arguments far more convincing now than they
4 were before. I thought they were a little bit -- they
5 weren't rigorous. And I think it's quite rigorous now. I
6 think that, although it may be beyond -- somewhat beyond
7 your charge, I think it would be very helpful in the
8 scientific literature in general if Dr. Hnizdo could
9 author or coauthor a letter to the journal in which your
10 paper was originally published clarifying this point in
11 the peer-reviewed literature.

12 The issue -- the second issue, which seems to --
13 well, let me ask you a question about Churchyard. One of
14 the I things as I read the revision is I wondered why it
15 was not possible also to do a calculation with the
16 Churchyard data.

17 DR. COLLINS: We'd have to contact him. He has a
18 figure with bar charts and showing a response. The thing
19 is, I don't -- he doesn't share the raw data. So we'd
20 have to contact him. And I can do that and see.

21 PANEL MEMBER BLANC: Because it would certainly
22 strengthen the section wherein you have -- which was in
23 the previous document, where you have sample calculations
24 with their papers.

25 DR. COLLINS: Right. But I would really need to

1 get ahold of the author, because it's just -- it's like a
2 percent silicosis. I don't know what the different --
3 with each exposure group, what the numerator and
4 denominator are.

5 PANEL MEMBER BLANC: Well, if it's possible -- I
6 mean since it's a recent paper, the person should be
7 contacted --

8 DR. COLLINS: Oh, yeah, his E-mail's in the paper
9 and --

10 PANEL MEMBER BLANC: And I would say that if you
11 can't get the data, you might want to say explicitly we
12 were unable to do this calculation with Churchard's data
13 because we -- the data weren't presented in a form that
14 allowed you to do it. Because it's -- it's sort of one
15 expects seeing it now. Then you say, "Well, that sounds
16 like a pretty rich recent data set." So --

17 CHAIRPERSON FROINES: What's the percent silica
18 in the Churchyard paper?

19 PANEL MEMBER BLANC: What's that?

20 PANEL MEMBER HAMMOND: Twenty percent.

21 PANEL MEMBER BLANC: It's similar to the --

22 PANEL MEMBER HAMMOND: No, 12 percent. Excuse
23 me.

24 PANEL MEMBER BLANC: -- the -- I mean it's within
25 range of the other estimates. It's reasonable.

1 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

2 SALMON: Most of the more modern studies actually report
3 lower percentages of silica than the Hnizdo and
4 Sluis-Cremer data.

5 CHAIRPERSON FROINES: Can I interrupt, Paul, just
6 for a second if you'll defer.

7 PANEL MEMBER BLANC: Yes.

8 CHAIRPERSON FROINES: That was a question that I
9 had for you.

10 If you took the study that you used primarily
11 with the 30 percent estimate of silica and said, based on
12 the current literature as we understand it, what would
13 you -- what would you conclude is the percent silica that
14 you're seeing?

15 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

16 SALMON: The range we see is something between 12 and --
17 12 at the low end and 30 at the upper end for whole dust.

18 CHAIRPERSON FROINES: Because in Vermont we had
19 used 9 percent for granite sheds. And so it's 9 percent
20 as far as I know to -- what was the upper bound?

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: Well, the upper value that we have in the range
23 in fact is the 30 percent, which Hnizdo reported. That
24 may reflect conditions in the mine. It may also reflect
25 that the more modern methods which depend on things like

1 x-ray defraction, which is, you know, a more certain
2 identification of silica, in fact are saying that the
3 earlier methods somewhat overestimated the amounts of
4 silica in the dust.

5 CHAIRPERSON FROINES: Yeah, it's always been a
6 problematic issue to relate particle number, et cetera, to
7 particle mass. And so that always has been -- Bill
8 Burgess always taught me that one couldn't trust those
9 kinds of measurements. And so I understand that x-ray
10 defraction method clearly is superior.

11 So you would argue then, you're talking as a
12 central tendency, somewhere around 20 percent, is that
13 reasonable?

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

16 CHAIRPERSON FROINES: Sorry, Paul.

17 PANEL MEMBER BLANC: No, no. And I think that
18 just underscores why -- if you could do the Churchyard
19 data, it would reinforce the entire argument, I think.

20 The other substantive issue that the comments
21 seem to be concerned with are whether or not the
22 mathematical calculations, even if correct, yield a result
23 which is biologically plausible, because of this argument
24 about sometimes air levels of ambient silica have
25 approached this value.

1 And although I think that you address that, I
2 think perhaps the document is still a little sheepish in
3 that regard. And I wonder if there are ways of presenting
4 the argument more forcefully. I mean you have two
5 arguments, one of which I think is not necessary and not
6 convincing, which is that there may be undetected
7 environmental silicosis. I mean I think that there may be
8 some undetected silicosis, for example, in agricultural
9 jobs which end up exposing people to pretty high levels of
10 silica that's not appreciated.

11 But the point is not that. The point is that in
12 fact your value is intended to be a value at which were
13 someone to be exposed lifelong at this value or above all
14 the time, that's the point at which you would -- above
15 which you might start to see an appreciable risk. So if
16 sometimes people have detected values that may be near
17 this for presumably transient periods, it in fact in no
18 way suggests that this is not a biologically plausible cut
19 point.

20 Now, you try to say that. But I think you should
21 go back over it and really look, because I think you --
22 because if in the same breath then you start to say well
23 maybe we're missing some cases silicosis, you're
24 undermining your own argument, I think.

25 Is it really true that the only -- you only have

1 one citation that you could make of anybody ever doing
2 ambient environmental silica levels? I mean you quote
3 these three samples all done in one study in one part of
4 Santa Barbara County. So nowhere else in the world?

5 DR. COLLINS: There were some. But we felt that
6 was the most reliable thing. The EPA 20-years ago had
7 some measurements, but --

8 PANEL MEMBER BLANC: And no one else anywhere has
9 ever --

10 DR. COLLINS: -- find getting it published is the
11 trick.

12 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
13 SALMON: One of problems is that there haven't -- really
14 haven't been very many measurements of real background
15 levels. For instance, the EPA measurements that Jim
16 referred to, most of those actually are I think what you
17 would characterize as near-source type of background
18 measurements rather than real backgrounds.

19 PANEL MEMBER BLANC: And how high do those ones
20 go.

21 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

22 SALMON: Some of them go, I believe -- 6 or --

23 PANEL MEMBER BLANC: And those are near source?

24 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

25 SALMON: Yeah, they're in the -- you know, they're sort of

1 the general vicinity of things that were going on kind of
2 measurements. The trouble is people have tended not to be
3 terribly interested in --

4 CHAIRPERSON FROINES: Kathy, did you want to
5 make --

6 PANEL MEMBER HAMMOND: Yes, but were those PM10
7 measurements, the EPA measurements? They almost certainly
8 were PM10 or total suspended particulate, right?

9 DR. COLLINS: I'm not sure. I'd have to --

10 PANEL MEMBER HAMMOND: Yeah, I mean they weren't
11 doing PM2.5 twenty years ago. So dollars to donuts, it's
12 either total suspended particulate or PM10, in which case
13 it overestimates the respirable. So I think that that's
14 also important, and all those environmental measurements,
15 to be very clear what that size fraction is.

16 PANEL MEMBER BLANC: Is that Also true of the
17 Santa Barbara measurements?

18 PANEL MEMBER HAMMOND: Those are probably PM10.

19 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

20 SALMON: Those were PM10.

21 PANEL MEMBER BLANC: Well, then that --

22 PANEL MEMBER HAMMOND: That needs to be clear in
23 the document.

24 PANEL MEMBER BLANC: Yeah. But then in fact the
25 statement that ambient levels have been near these levels

1 is not true, because these ambient levels were
2 significantly lower.

3 So I would just say that it's not -- this is a
4 comment somewhere -- somewhere in between style and
5 content. I mean I think it's an important content
6 question because it uses an argument to say this is in the
7 biologically plausible end result that you have. And I
8 think that that is an important question to ask oneself.

9 For example, we've had previous documents that
10 we've looked at where the calculations in the NK values
11 which seem in a range that is not plausible, because were
12 that to be the case, we should be seeing more diseases.

13 So I think it's not a weakness of your
14 calculation. It's simply you don't put the best, most
15 coherent argument on it.

16 So those are the major things.

17 A couple of minors things. One is that when you
18 do your ILO category, Table 1, you're citing the paper
19 that I did with Gordon Gamsu -- you know, that 0 over 1 is
20 possible silicosis. The citation for what the ILO
21 criteria should be should be the ILO criteria document,
22 not a secondary analysis question, because that's what we
23 based on. So that's just slightly sloppy.

24 And, you know, thanks for putting in sandblasting
25 as a source of ambient silica, because I think that is

1 relevant. I guess I think sandblasting is a pretty
2 important occupational source too. And it's really not in
3 the first list, unless you mean sandblasting when you talk
4 about as an abrasive. If that's what you mean in that
5 phrase, then I would put e.g., sandblasting.

6 And then I think you're -- you've tried to expand
7 your human health effects list to be a little bit more
8 inclusive and I think that's good. That being said -- and
9 also your sort of theoretical model of the path of
10 physiology of it. I think that there should be some kind
11 of nod to acute silicosis, even though it's not relevant
12 to what you're doing here, since you're being fairly
13 exhaustive in your list of human health effects. Since
14 acute silicosis, which is pathologically the same as
15 pulmonary alveolar prognosis.

16 And, secondly, I think that you need to state
17 that -- as you get beyond the part about silica particles
18 are engulfed by macrophages, I think you have to say
19 something like "The generally assumed pathological model
20 is" or something like that. I mean you state this as if
21 this was, you know -- I mean these are constructs and data
22 support it, but it's still the presumed -- you know, based
23 on experimental evidence.

24 So those are I think the main things that -- the
25 two main things. But I think that in general, the

1 document is considerably stronger by taking head-on the
2 issue of the sampling and what your standard refers to, I
3 mean how it would have to be interpreted.

4 And the inclusion of the more recent data and
5 some of the relevant older data. And then the analysis
6 related to the silica content.

7 And in particular, the part where if you did the
8 calculations with the 30 percent, it comes out to the
9 exact numbers that someone else had having worked with the
10 data independently. That doesn't seem like that would be
11 likely to be due to chance.

12 DR. COLLINS: It might be incidence, according to
13 Dr. Gibbs.

14 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

15 SALMON: We don't believe in coincidences.

16 PANEL MEMBER BLANC: Well, can I ask: Were these
17 numbers like -- I mean these were to the two digits past
18 the decimal point, right? So is that -- do you feel
19 you've said that as clearly as you can at that point in
20 the document?

21 SUPERVISING TOXICOLOGIST MARTY: We can go back
22 and look and see if we can make that clearer.

23 PANEL MEMBER BLANC: Because to me that was
24 the -- the whole thing was logical, but that was sort of
25 the coupe de grace as I read it. But it wasn't -- I mean

1 I think it would be clearer that the -- it can't -- it's
2 not an artifact because this person went back -- had gone
3 back to the original data, all right, as I understand it.

4 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

5 SALMON: Yes.

6 PANEL MEMBER BLANC: So I'm done.

7 CHAIRPERSON FROINES: Kathy.

8 PANEL MEMBER HAMMOND: First, I would really like
9 to commend OEHHA for tackling this incredibly difficult
10 problem of this percent silica and what was going on. And
11 I was -- read through your materials and the supporting
12 materials and the papers. And that was real detective
13 work, a lot of work. And so that was really good. And,
14 like Paul, I found it very convincing in the end. But it
15 was a lot of work. And in the end of course the fact that
16 the author, the original key study felt that that was
17 appropriate I think is very important. I think that's
18 nice you were able to contact her.

19 I think there are a couple of other things. Even
20 though you don't deal with it in the document, but -- you
21 know, in the Gibbs paper, he -- the authors, Gibbs and Du
22 Toit, say over and over that there's like a twofold or a
23 fourfold decline over time and underestimate of exposures,
24 and they go through that. But when I went back and looked
25 actually at the data, like their Table 2, the historical

1 data does not bear out what they were saying. It's true
2 that from the first year they have in the study, 1931, to
3 the end, there looks like to be a twofold change. But
4 that change almost entirely occurs in the first three
5 years before people entered the study.

6 So if you take the time when people entered the
7 epidemiologic study and you looked at that change over
8 time, there's very little change. In fact I would argue
9 there's no discernible change.

10 So if you go over 1940, or even from 1934 to
11 1967, there's virtually -- you know, there's no --
12 certainly no significant change, particularly if you go to
13 their Table 5, and from which they do give -- it's not in
14 Table 2 unfortunately. And there's no indication of the
15 precision of these numbers. And there's actually a very
16 wide variation, as we expect in the occupational setting.
17 So if you look at this coefficient of variation, Table 5,
18 which is not calculated, but I did calculate, you know,
19 for the very first measures of coefficient of variation
20 was 50 percent. But after that the coefficient of
21 variation is basically 80 to 90 percent. You know,
22 there's a pretty huge curve.

23 So that to be sitting there given that and saying
24 in Table 2 that when you go from 118 -- actually the total
25 overall in 1941 was 118 -- you go to 128 in 1967, that's

1 hard to say that's a decline. I think that by itself is
2 an increase. But, you know, the 118 could be 139 to 128,
3 given the microscope differences.

4 But, you know, this -- I actually see an amazing
5 evidence of stability and very little change. It probably
6 does go up and down with production. So I know that comes
7 with detail, but I think it's part -- it's part of that
8 history. Because as an industrial hygienist too I'm used
9 to thinking that there have been huge changes over time.
10 That's my first thought. We often look at threefold and
11 fourfold and fivefold and tenfold changes over time. And
12 these are actually amazingly stable over time. And I
13 think that's actually noteworthy to the degree we have any
14 data.

15 And actually they also mention in the paper the
16 two main reasons the levels are relatively low and stable
17 are that from 1911 they've been using wet mining
18 procedures, as opposed to the dry methods often used. So
19 that suppresses dust.

20 And they also, because it's so deep -- the mines
21 are so deep, they're very hot, they have to have a lot of
22 ventilation. That reduces the dust. So I thought that
23 was actually very interesting to see.

24 So all of those things in combination with all
25 that you have done convinced me that those numbers are

1 correct.

2 The other question about the percent of silica in
3 the dust, actually as I looked through the various data,
4 including -- this was -- a lot of it as summarized in the
5 Churchyard data, I actually see a lower percentage than 30
6 percent. In fact, 30 percent's the only place I see it,
7 is in the key study. And as I look at the data, the
8 Randall data and all the data that's been cited, I see
9 numbers between 10 and 20 percent and nothing above 20
10 percent, which would actually imply just the opposite
11 problem from what Gibbs is talking about.

12 So if there's any error, I think it's running the
13 other way. And I would just comment on that. But, you
14 know, you have to make the --

15 CHAIRPERSON FROINES: Well, the implication of
16 that is that REL is too high.

17 PANEL MEMBER HAMMOND: Right.

18 PANEL MEMBER GLANTZ: Well, wouldn't -- going
19 back to the early discussion about 30 percent versus 20
20 percent versus 9 percent. If you were to take the central
21 estimate of 20 percent, wouldn't that push the REL up?

22 PANEL MEMBER HAMMOND: No, down.

23 PANEL MEMBER GLANTZ: I meant down.

24 PANEL MEMBER HAMMOND: Well, see, the trouble is
25 Gibbs is saying it should be 54 percent. That's the other

1 number in the mix. But, I mean, it just doesn't fit any
2 other data.

3 And I think the other piece is that, as far as I
4 can tell -- and I would actually like to have the table --
5 I think I mentioned this to you earlier -- a little
6 clearly on the methodology. But as far as I can tell,
7 it's only the Churchyard data that has x-ray defraction
8 for the silica. And that's the one that has the lowest
9 number -- well, among the lowest, 12 to 16 percent was
10 what they found. So I tend to take that particularly
11 seriously. And then there's no evidence of change from
12 when they started listing data from '77. It was 10 to 20
13 percent in '77, '87 to '88 it was 10 to 20 percent, '92 to
14 '94 surveys were 15 percent -- 12 to 16 percent. So it
15 just looks like it's in that 10 to 20 percent range. And
16 20 percent's the upper end of that.

17 CHAIRPERSON FROINES: I mean going back to Gauley
18 bridge, if you want -- Paul and you will at least know
19 what that was -- you know, the percent silica was very,
20 very high. So that there are historical examples of --

21 PANEL MEMBER BLANC: Would you say that
22 G-a-l-l-e-y?

23 CHAIRPERSON FROINES: What?

24 PANEL MEMBER BLANC: Galley Bridge, G-a-l-l-e-y?

25 CHAIRPERSON FROINES: G-a-u-l-e-y.

1 PANEL MEMBER BLANC: G-a-u-l-e-y.

2 PANEL MEMBER HAMMOND: Hawks Nest.

3 PANEL MEMBER BLANC: Thank you for the spelling.

4 PANEL MEMBER HAMMOND: So, anyhow --

5 CHAIRPERSON FROINES: But my point is in general
6 what one has found has been lower than those values, not
7 higher.

8 PANEL MEMBER HAMMOND: Yeah, in the miners.

9 Now, the second -- my second major point is the
10 Churchyard study, which I know came out since your first
11 assessment -- and I'm not sure just what the appropriate
12 way to include this is, but I would just like to comment
13 on it -- I found that study very sobering when I read it.
14 I mean it's just really quite sobering. And it's notable
15 both for the quality of the exposure assessment in the
16 study, although they have some of the best data included
17 in the x-ray defraction data, and for the magnitude of the
18 effect that's seen. And so they actually collected
19 respirable dust, weighed it gravimetrically, and then
20 analyzed it by x-ray defraction.

21 So they didn't deduce it, which was done in the
22 other methods. And all of the deductions and
23 subtractions, I think most of the errors would lead
24 towards overestimates of percent silica. So if you just
25 were to look at the directions of errors, they would lead

1 to an overestimate, which I suspect the 30 percent numbers
2 are in the other studies.

3 They also have documented very little change in
4 the overall exposure during the relevant time period for
5 the people in the study.

6 And there are two major epidemiological -- well,
7 first of all there are about 20 percent of the workers --
8 it's a cross-sectional study. The workers average age 46,
9 and 20 percent of them have silicosis by the ILO 1 over 1.
10 And I would defer to Paul or someone else about the
11 significance. But half of those have two or three. You
12 know, so that's a more severe silicosis, right?

13 So that seems rather sobering to me that at a
14 relatively young age, on 21 years of exposure, they have
15 that effect.

16 But, furthermore, because it's a cross-sectional
17 study, it has two limitations:

18 The first is that any people who got sick or even
19 were out on sick leave for a cold or for any other problem
20 were not included in the study. The cross-sectional
21 measurement of this just excluded people who are out on
22 sick leave or who might have left work because they'd
23 gotten sick already. So that already depresses -- that
24 will underestimate any effect.

25 And, secondarily, because it doesn't have -- this

1 isn't the follow-up after all these years of exposure. We
2 all know, as you well cited in the document, the internal
3 dose continues for silica, that everyone knows that those
4 particular category of workers will have a higher rate of
5 silicosis ten years out than what's seen at this point.
6 And that's already 20 percent.

7 So with even those problems, I found it a pretty
8 sobering study.

9 Also the silica exposures averaged 53 micrograms
10 per cubic meter, half of the standard -- the current OEL's
11 in most of the world. And they said that 90 percent of
12 the workers had average exposures between 29 and 75
13 micrograms per cubic meter. So these people had a low --
14 in the world of what the standards were, relatively low
15 exposures, and 20 percent of them as an underestimate had
16 this already.

17 So I found that a rather sobering study. And if
18 there were a way to incorporate it without leading to a
19 lot of difficulties, I would encourage you to. But I
20 don't think that should slow down the process. And if
21 that slows down the process, we could just note the
22 importance of the study that came out after the main
23 documents.

24 CHAIRPERSON FROINES: Have you done a calculation
25 of what that would lead --

1 DR. COLLINS: We can't do it because of the way
2 the data's written. It's a bar graph with percent
3 silicosis. And all we can find out are the numerators and
4 denominators from the authors.

5 PANEL MEMBER HAMMOND: That's who they'd have to
6 contact, the authors.

7 CHAIRPERSON FROINES: Well, that wouldn't be a
8 terrible idea. This isn't -- this is a very important
9 chem --

10 PANEL MEMBER HAMMOND: Yeah, I think the study
11 itself was a very important one.

12 Then the other issue which we spent so much time
13 on last time was the metric to use, the size. And I
14 commend you in terms of scientifically going to the
15 respirable as defined in the occupational method, which is
16 the way in which the sampling was done for the critical
17 studies. And I think that that's totally appropriate.

18 I think it's better to refer to it as the ACGIH
19 method or the ACGIH/ISO method for definition of
20 respirable, because NIOSH just refers themselves to the
21 ACGIH.

22 I think that in the documents still there are
23 some points of confusion. I mean you point out that in
24 the environmental community, people often use the term
25 "respirable" meaning PM10. So I think that maybe having a

1 paragraph early in the document, that just is very clear,
2 that says, "This 'respirable' term is myth. It has these
3 multiple meanings. In this document we are going to use
4 respirable" -- and maybe italicize it -- "always meaning"
5 you know, with the occupational definition, go through
6 what that is, and say that instead of -- even though PM10
7 is referred to as respirable, just call it PM10, because
8 there's a name for it -- another name nor it. And use
9 PM10 throughout. And I would just suggest you do a search
10 and just check for all words "respirable" and keep that
11 very clear throughout to do that.

12 And as I mentioned earlier, I think it's
13 important to clarify the size distribution that was used
14 for the ambient measurements that were taken. My guess is
15 they're either TSP or ambient -- PM10.

16 I think the recommendation for the REL, it's
17 there, but I think it needs to be very clear. As I
18 understand what you're suggesting is that this REL, as you
19 said here, is for respirable particles as defined in the
20 occupational setting. And you can go through that.

21 And the PM10 samples can be taken as a screening
22 tool, because they over -- they'll overestimate. They
23 shouldn't be seen as a problem, but tell you where you
24 need to do more. And I think that's in your document, but
25 not always clear to all the readers.

1 And like page 33, the first two lines are kind of
2 confusing, whether you're saying -- I think at one
3 sentence you're using respirable for ACGIH and one
4 sentence it's about PM10.

5 And then I have a series of just tiny little
6 comments. Occasionally -- most of the places you've got
7 it corrected, but occasionally you're still -- there's a
8 mention about the ACGIH definition relating to respirable
9 as being a deposition. But it's actually a penetration of
10 particles of a certain size to the lung. So just kind of
11 check some of those.

12 The WHO recommendation that you cite, is that for
13 occupational or environmental, the 40 micrograms per
14 cubic --

15 DR. COLLINS: I think -- I'm pretty sure that's
16 occupational.

17 PANEL MEMBER HAMMOND: Occupational.

18 And then what particle size were they -- did
19 they specify --

20 DR. COLLINS: I don't remember right now.

21 PANEL MEMBER HAMMOND: I think it should be in
22 the document. If you could just put that -- and those are
23 small things. But just -- if you're going to cite it, I
24 think given those things we need to say to whom it applies
25 and what size range.

1 Oh, and I guess one other -- and, again, I would
2 defer to some of the physicians here. In the American
3 Chemical Council statements, they said that idiopathic
4 small irregular opacities of non-occupational populations
5 have been reported in the literature of the pool
6 prevalence 1.3 percent in North America. That's in their
7 comments.

8 Does that mean that there is a --

9 PANEL MEMBER BLANC: Well, I think they do
10 attempt to go back. And there is a section in the revised
11 document where they have an expanded discussion of the
12 very low prevalence of opacities which could be graded by
13 ILO criteria. And you cite the Castellán study. And it's
14 quite low. And almost all of what is seen as a sort of
15 background prevalence is 1 over 0, not 1 over 1.

16 PANEL MEMBER HAMMOND: Oh, okay.

17 PANEL MEMBER BLANC: So they're, you know --

18 PANEL MEMBER HAMMOND: That's what they meant
19 by -- I just was curious. I wasn't sure about it in --

20 PANEL MEMBER BLANC: And Much of it's not -- much
21 of it's irregular and not rounded.

22 In any event, I thought there was enough it and I
23 thought there was enough of a discussion there, now in the
24 expanded version, as you --

25 PANEL MEMBER HAMMOND: But I think that you've

1 done a great job on this document. A lot of work has gone
2 into it.

3 Thank you very much.

4 DR. COLLINS: Thank you.

5 CHAIRPERSON FROINES: So having heard from the
6 two leads, why don't we go around the room and give other
7 comments. I have some comments, but I'll defer.

8 Stan.

9 PANEL MEMBER GLANTZ: Well, I have one -- I read
10 it through. This is not my area of total expertise. But
11 I had one small question.

12 (Laughter.)

13 PANEL MEMBER GLANTZ: And then I had a comment
14 based on the discussion so far. And let me just -- this
15 is a very picky point. But somewhere here --

16 CHAIRPERSON FROINES: We understand that when you
17 say this is not your area of expertise, everybody starts
18 to shutter.

19 (Laughter.)

20 PANEL MEMBER GLANTZ: Why?

21 CHAIRPERSON FROINES: Because we don't know
22 what's coming next.

23 PANEL MEMBER GLANTZ: No, it's a very small
24 thing.

25 If you just look on page 26, you have a P value

1 by a Fisher exact test. And I think you should specify if
2 that's one or two tails. Hopefully it's two tails. You
3 should use the two-tail test there. But a lot of programs
4 report one-tail tests without telling you. That was my
5 highlight subjectively.

6 The question I had based on the discussion -- I
7 mean I also thought you did a very nice job of responding
8 to the comments and dealing with this 30 percent issue.
9 And I came in here all happy about that. But now
10 listening to the conversation, I'm wondering if you
11 shouldn't be using 20 percent.

12 PANEL MEMBER BLANC: No.

13 PANEL MEMBER GLANTZ: No. Okay.

14 So you're happy with the 30 percent?

15 PANEL MEMBER BLANC: Yeah.

16 PANEL MEMBER GLANTZ: Okay. Then I'm happy too.

17 PANEL MEMBER BLANC: I think it's fine enough to
18 say that, if anything, it's conservative, it's not
19 radical. But I don't think that there is a scientific
20 basis for presuming it to be lower than what -- to doing
21 the calculations a little bit lower. I think they should
22 stick with what they have.

23 CHAIRPERSON FROINES: I'm not sure Kathy would
24 agree with that --

25 PANEL MEMBER HAMMOND: Yeah, I guess I don't. I

1 mean -- the thing is, every other -- the better the data
2 are -- any place one looks at the data, the better they
3 are, the more it looks like it's between 10 and 20
4 percent. And the only place I see 30 percent is when it's
5 this very crude way they did it. You know, where you
6 just --

7 PANEL MEMBER BLANC: But you have to use the --

8 PANEL MEMBER HAMMOND: -- you kind of -- you acid
9 wash it and you kind of heat it up to see what's --

10 PANEL MEMBER BLANC: Well, then if you don't
11 believe the data, then you shouldn't use the study. I
12 mean if you're going to say, okay, we're going to use the
13 study with its strengths and with its weaknesses, then you
14 use the data that you have. And then that's why they have
15 these other calculations from other studies. I guess
16 it's -- we didn't specifically comment on the important
17 revision in that section, which is that when you use the
18 Hughes study in this revision, you have gone from yielding
19 a value of 10 to yielding a value of 3, which is again
20 matching what you've gotten. And that was based on the
21 fact that the author's no-effect level was really a
22 lowest-effect level.

23 And then you say, "See below." What's the
24 "below" supposed to refer to?

25 DR. COLLINS: I'm pretty sure that it was a --

1 because of some of the extra discussion, it goes further
2 down. And the second supportive study, Hughes, is all
3 down. In this case the silicosis is the lowest exposure
4 group. And then we basically say we believe it's a LOAEL,
5 not a --

6 PANEL MEMBER BLANC: I know. But where is the
7 "see below" -- where is the reader supposed to look
8 below --

9 DR. COLLINS: Oh, oh, yeah. Yeah. Okay.

10 PANEL MEMBER BLANC: What is it that you're
11 referring to?

12 DR. COLLINS: There's a paragraph --

13 PANEL MEMBER BLANC: On the next page?

14 DR. COLLINS: Well, no it's actually after Table
15 20. It's second -- it actually got moved a lot because we
16 had put in this new section. Maybe that's what makes
17 it --

18 PANEL MEMBER BLANC: Yeah. So I think that needs
19 to be --

20 SUPERVISING TOXICOLOGIST MARTY: We'll fix that.

21 PANEL MEMBER BLANC: -- reedited. And I think
22 that that -- you know, it's a major issue.

23 SUPERVISING TOXICOLOGIST MARTY: I have a
24 suggestion for revision to deal with this issue of percent
25 silica. We can, I think -- you know, we feel we need to

1 stick with the study. But it seems clear to me that we
2 should be making a statement that this is in no way an
3 overestimate of the REL based on methods to look at
4 percent silica in the dust. And then note what Kathy has
5 noted herself, that the better the methods and the newer
6 the studies, the lower these percents seem to be. At
7 least what we would be doing is pointing out that
8 perhaps --

9 PANEL MEMBER BLANC: No, no. And I would support
10 that. I think that's a reasonable thing to do. Because,
11 again, you're talking about the -- in this case not the
12 biological plausibility, but the sample.

13 CHAIRPERSON FROINES: Yeah, I want to go on
14 record basically agreeing with Kathy, that I think that
15 the estimates of 30 and certainly 54 percent seem to me to
16 be high. But I think that we shouldn't necessarily change
17 the study that we're relying on. I think that the -- that
18 language that Paul and you were talking about would make
19 sense.

20 PANEL MEMBER BLANC: I guess one other -- no,
21 never mind.

22 Well, let me just ask the question. In the Chen
23 study of tin miners, it was also based on the ILO-graded
24 x-rays, I assume?

25 DR. COLLINS: I think it was -- it was based on

1 the Chinese system, which is similar.

2 PANEL MEMBER BLANC: Since tin causes
3 radiographic opacities, how did they account for --

4 DR. COLLINS: They didn't mention anything about
5 tin or stenosis anywhere in the study. I went through it
6 and I couldn't find any references to that.

7 PANEL MEMBER BLANC: Because I had asked about
8 this before and --

9 DR. COLLINS: Yeah. I couldn't find anything.

10 PANEL MEMBER BLANC: Then how do use that study?
11 I mean does that cause the same problem as the coal miner
12 study?

13 DR. COLLINS: I don't think so, because it was --
14 they had lots of -- they had lower levels. They had a
15 whole gradation of levels of exposure. But I mean as far
16 as is there a one-to-one correspondence between the
17 Chinese system and the ILO, I'm not sure. They said it's
18 a similar system. And they were collaborating with the
19 people from either -- I think NIOSH on it. So it wasn't
20 just -- they had input from people that would be familiar
21 with the American system.

22 PANEL MEMBER BLANC: Yeah, that's not my point.
23 I mean you could use the ILO -- they could have used the
24 ILO too. But if you use the system where you're looking
25 at radiographic opacities in people who are tin miners,

1 which is another cause for having radiographic
2 opacities -- remember, the whole point of the ILO system
3 is radiographic opacities which can be consistent with
4 pneumoconiosis. It's not a diagnostic system you've
5 revised, to make that clear.

6 DR. COLLINS: I went back and looked at that tin
7 miner study. And there was no mention of any disease
8 caused by tin. The only thing they discussed was
9 silicosis. And, now, should they have? I don't know.
10 But I could not find any reference to anything other than
11 silicosis.

12 SUPERVISING TOXICOLOGIST MARTY: I think at a
13 minimum we need to in the description state that tin
14 exposure can also cause radiologic opacities, when we
15 discuss that study. Whether or not the authors themselves
16 make mention --

17 PANEL MEMBER BLANC: Well, I mean I just wonder
18 whether there are -- whether if there are certain
19 questions about it that can't be clarified, I don't think
20 you should drop the study from the document. But should
21 it be one of the studies that appear as the four
22 studies -- the three other studies which are supported?
23 Because the problem with it is it could go either way.
24 You could be overestimating or underestimating silica
25 effect, because of the people who had higher tin exposure

1 had lower -- if there was a systematic -- weird systematic
2 relationship that could lead you to overestimate the
3 silica effect or underestimate the silica effect,
4 depending, right? I mean I can't predict how it could
5 confound a relationship.

6 CHAIRPERSON FROINES: Stan?

7 PANEL MEMBER GLANTZ: That's all I had.

8 CHAIRPERSON FROINES: Good. I'm glad you raised
9 that point, but it actually took us to a somewhat better
10 place on this issue.

11 Joe?

12 PANEL MEMBER LANDOLPH: I think Kathy and Paul
13 did a fantastic job and everybody else. And I think that
14 we all did a fantastic job leaving that -- but I'm
15 satisfied with the document.

16 CHAIRPERSON FROINES: Charlie, I don't know if
17 you've had a chance to look at this.

18 PANEL MEMBER PLOPPER: I did.

19 CHAIRPERSON FROINES: You did.

20 PANEL MEMBER PLOPPER: I thought it was an
21 excellent document. The only concern I had is that it was
22 underestimating the risk based on the percentages. But
23 that sounds like it was everybody else's concern also.

24 CHAIRPERSON FROINES: Craig.

25 PANEL MEMBER BYUS: I have nothing to add.

1 That's very nice. And you've dealt with all the comments
2 very effectively.

3 CHAIRPERSON FROINES: I have a couple questions.
4 It won't take long.

5 First, I was interested in your references,
6 because there are two references to a fellow I worked with
7 in Vermont years ago named Jack Craighead. And so I've
8 been through the document and I can't find -- there are
9 references to Craighead, but I can't find any discussion
10 of his work.

11 The reason I raise the issue is Craighead was one
12 of the first people who showed actual pathologic changes
13 in the lung associated with very relatively low levels of
14 silica exposure. We got autopsy victims and took out
15 lungs and looked at people who had very low silica levels
16 at that point, people who had worked in industries where
17 the silica was well controlled. And Jack saw and wrote
18 papers about what he found in terms of changes.

19 So I think that in terms of going to the issue --
20 there's this issue that, as we all know, that John Peters
21 has argued for some time that one sees lung function
22 changes before radiographic changes. And so if
23 one measures -- if one develops standards based on lung
24 function changes, you would have perhaps different
25 numbers. Craighead argued that you see level -- you see

1 changes at very low levels as well.

2 And so there are some other ways people have
3 looked at the issue. And so the fact that there's the
4 references but no discussion of those kinds of questions
5 seems to me -- I mean either take out the references or
6 put in some text is what I think you need to do.

7 DR. COLLINS: I remember distinctly, one of the
8 Craighead references he had studied 12 slate-exposed
9 people and found some changes in the lung, but wasn't sure
10 it was pneumoconiosis. But it was a lung effect due to
11 slate exposure.

12 CHAIRPERSON FROINES: Well, there's some other
13 literature, I think.

14 DR. COLLINS: That may well be.

15 CHAIRPERSON FROINES: I don't -- I think what
16 you've done is -- as everybody agrees, is more than
17 sufficient. But having worked regulating the granite
18 industry in Vermont, the issue of lung function changes,
19 and pathologic changes at low levels is still a matter of
20 interest to me. So I -- but I don't think you need to go
21 back and put that in. I think what you have is
22 sufficient.

23 I had one question about a response that was
24 written that talks about the USEPA -- this is on Culver 4.
25 "The USEPA defines a reference concentration as an

1 estimate, with uncertainty spanning perhaps in order of
2 magnitude of a daily exposure," and so on and so forth.
3 "OEHHA uses a similar definition. The 'order of
4 magnitude' statement can be taken as a confidence level."

5 Now, I found that sentence -- this sentence to
6 be -- I don't know what you're saying. And if you're
7 saying that --

8 DR. COLLINS: Did we say it or we -- we said it
9 in our response.

10 CHAIRPERSON FROINES: This is in your response.

11 If you're saying that you accept -- that you
12 assume that you have an order of magnitude confidence --
13 rather uncertainty spanning an order of magnitude, then I
14 suspect that should be in your main document, if that's
15 what you're saying. But I don't think you're really
16 saying that.

17 It's Culver 4. And it says that "the 'order of
18 magnitude' statement can be taken as a type of confidence
19 level. OEHHA uses a similar definition for chronic RELs
20 in the technical support documents," so on and so forth.
21 And so you're essentially acknowledging EPA's order of
22 magnitude uncertainty value. And I think Dale Hattis just
23 rolled over dead, you know, from a statement like that.

24 The point being that -- well, that point's
25 obvious.

1 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

2 SALMON: It seems like we need to rephrase that.

3 CHAIRPERSON FROINES: Well, I think you need to
4 rephrase it simply because I don't think you mean it. And
5 I think that if you're going to talk about the magnitude
6 of uncertainty, then that ought to be appear in your full
7 document.

8 PANEL MEMBER BLANC: What did you mean?

9 DR. COLLINS: Probably I -- I copied the EPA's
10 definition, and should have put that sentence after the
11 EPA's definition rather than after ours.

12 SUPERVISING TOXICOLOGIST MARTY: The EPA makes
13 that statement. And it's really -- it's really not based
14 on any kind of statistical analysis. It's more of a
15 gestalt about the database available to do any of these
16 kinds of assessments. In the case of crystalline silica,
17 we have some very good data on which to base a REL. In a
18 lot of cases we have pretty poor data in terms of: What
19 toxicological endpoints were actually evaluated. Did they
20 look at exposure early in life? And what other -- you
21 know, what exactly are the studies you have to use to do
22 any type of quantitative estimate?

23 So that statement appears in EPA's documents just
24 to give the idea that these types of calculations are not
25 perfect by any stretch. But I don't think anybody means

1 it in a statistical sense of a confidence bound or --

2 CHAIRPERSON FROINES: Yeah, unfortunately it says
3 that it's found in here as a confidence bound. And so I
4 don't think you're really saying that your values
5 should -- could be in a range of .3 to 30.

6 SUPERVISING TOXICOLOGIST MARTY: No.

7 CHAIRPERSON FROINES: And I don't think that's
8 what you're saying.

9 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF
10 SALMON: No.

11 CHAIRPERSON FROINES: So I think you ought to
12 take a look at that and maybe improve on it.

13 I want to go back to this issue that we debated
14 so long and hard last time, because I -- and this gets us
15 a little beyond the issue of risk assessment. But I think
16 it's an issue that's come up.

17 And, for example, here you say -- on IDPA 5 you
18 say, "CARB and the air districts have regulatory
19 approaches designed to provide the best possible
20 protection for public health, taking into account the
21 specific features of each individual situation."

22 PANEL MEMBER BLANC: Are you talking about a
23 response somewhere?

24 CHAIRPERSON FROINES: Yeah.

25 PANEL MEMBER BLANC: What page are you on?

1 CHAIRPERSON FROINES: IDPA 5.

2 And so, Melanie, the issue I still am concerned
3 about is we no longer are talking about PM10 as the
4 operative sampling method for identifying silica. And you
5 talk about using the NIOSH respirable method. But I don't
6 know -- I don't understand -- and this may be me and not
7 you -- but I don't understand then what ARB is going to
8 use to measure silica, because the NIOSH sampling method
9 is not what they're going to use. So the NIOSH
10 definitions -- and Paul's spoken to that issue -- is
11 something that one can acknowledge in the context of the
12 risk assessment.

13 But what's the practical significance of that at
14 this point? What are you going to do? You've got this
15 wonderful table in here showing cutoffs with various
16 sampling devices. And so how is one going to determine
17 what the -- you know, when you've gone to Santa Ana and
18 Santa Monica and the winds blowing 30 miles an hour across
19 the beach, you know, how are you going to monitor for
20 those silica levels that are obviously quite high?

21 SUPERVISING TOXICOLOGIST MARTY: Well, I'm going
22 to speak for ARB now, which is probably not the greatest
23 thing. And maybe -- I know Lyn was in the audience
24 earlier. He might talk about this.

25 CHAIRPERSON FROINES: Well, Lyn's sitting right

1 there.

2 SUPERVISING TOXICOLOGIST MARTY: We've had some
3 preliminary discussions. And we think we need to set up a
4 working group to address this issue. Because, as you
5 note, ARB has standard methods for PM10 and now PM2.5, but
6 not something that's exactly analogous to the ACGIH
7 method.

8 So I don't know if Lyn wants to add anything to
9 that. But it's a good question.

10 ARB AIR POLLUTION SPECIALIST BAKER: Hi, Dr.
11 Froines. Lyn Baker with the Air Resources Board.

12 We've talked with Melanie and OEHHA staff about
13 this issue a few times, as Melanie mentioned. And we do
14 not have a method for measuring PM4. You could use the --
15 the studies have been done with a cyclone personal
16 sampler. It's a little device attached to a person's vest
17 or whatever. It measures PM4 at a very slow flow rate.
18 But it's designed for an occupational setting. And it has
19 not actually been validated for concentrations below 25
20 micrograms per cubic meter. So with the chronic REL
21 proposed at 3, if you used this in an ambient setting
22 you'd have to do some validation work to make sure it was
23 even a valid method. But currently we'd have to do some
24 side-by-side work with PM10 samplers or other samplers if
25 we were going to try to come up with a ratio or to design

1 a different sampler.

2 PANEL MEMBER BLANC: Well, I guess a couple
3 comments. And this echoes back to the discussion at the
4 last meeting. And now with the corrected language with
5 the document, in fact the response that John is referring
6 to on IDPA 5 is probably imprecise, because the OEHHA
7 staff realizes that the proposed REL is close to levels
8 that have been obtained with PM10, which is -- you know,
9 which would overestimate. So actually in fact we don't
10 have any evidence that there are ambient levels measured
11 consistently with what the REL is stated as that would be
12 close to 3. That's one point.

13 But the second point to being more -- less
14 bureaucratic, based on the size cutoffs it does seem that
15 ARB could at least develop an algorithm wherein if the
16 PM10 measurement is below 3, then based on the size cutoff
17 certainly the ACGIH-based sampling method, which NIOSH
18 concurs, would have to be also below 3. If you did
19 side-by-side monitoring and the -- both the PM10 and the
20 PM2.5 were above 3, then you know you're above 3 with --
21 you would be above 3 with NIOSH.

22 And the problem would be -- or where you would
23 need an algorithm for doing additional sampling would be
24 if you had a value which was above 3 on the PM10 and below
25 3 on the 2.5. That's the situation where you actually

1 would not know. You could have some algebraic, you know,
2 guestimates on -- you know, Dumont Carlo estimates or
3 something. But even -- I think you'd have to come up with
4 an alternative sampling method. But at least that would
5 be a useful screening algorithm.

6 ARB AIR POLLUTION SPECIALIST BAKER: It would.
7 And we've also thought about that, that it would probably
8 be pretty site specific. Or if that ratio in a --

9 PANEL MEMBER BLANC: Now, whether it's useful in
10 this document to say -- in this section wherein you talk
11 about what these various words, how they're used. But I
12 think if you wanted to say that if a sample -- you know,
13 the implication of the figure -- this figure on page -- is
14 it -- it's in the main document, right? The figure --
15 yeah, the last figure. The implication of that figure on
16 page 34 in fact is that if a value with a -- if a PM10
17 value were below 3, then the NIOSH value has to be below
18 3. And I think that would be a useful statement.

19 PANEL MEMBER HAMMOND: One thought I had is you
20 could actually modify this figure a little bit and just
21 have the PM10, PM2.5 and the occupational respirable
22 curves, and actually shade the areas between some of those
23 lines to emphasize this is the degree of overestimate --
24 of potential overestimate and of underestimate. But
25 without knowing the full particle size distribution -- and

1 not only the full particle size distribution, but the
2 composition could change with particle size. So I think
3 you have to be extremely careful. I don't think you can
4 use an algorithm. I think you have to do a measurement.
5 And I think you're absolutely correct, Paul, that you
6 could do --

7 PANEL MEMBER BLANC: -- screening?

8 PANEL MEMBER HAMMOND: The screening that you
9 outlined would work.

10 CHAIRPERSON FROINES: I think you'd have to do a
11 PM2.5.

12 PANEL MEMBER HAMMOND: But I would actually point
13 out as well that there -- you're right, that there are
14 these small personal sampling cyclones. But there are
15 also high volume cyclones that yield respirable dust, you
16 know. And I have one that's over 20 years old. I mean
17 they're not new. There are plenty of those out. So there
18 are ways to do respirable sampling. I know that they're
19 not in the standard repertoire of ARB. But you're not
20 limited just to the, you know, 1.7 liters per minute nylon
21 cyclone. There are other options that will go up 400
22 liters, you know, 430 liters and things like that.

23 CHAIRPERSON FROINES: And, Lyn, I agree with you,
24 that I think that the percent silica is going to be -- is
25 going to be changing quite considerably, depending upon

1 where you are.

2 So that I don't know if you want to -- I don't
3 know. What does the Committee think about whether or not
4 this discussion needs to be in this document? Or this is
5 something that we can do something at ARB, and OEHHA will
6 deal outside the scheme of this review and this Committee.

7 PANEL MEMBER HAMMOND: I think the document
8 stands as a scientific document as it is. But it does
9 present some pragmatic challenges to ARB. But I don't
10 know if those are too difficult to --

11 PANEL MEMBER BLANC: Well, but it is true -- you
12 could make a couple -- it is true, I'm not wrong in saying
13 this, that if a PM10 was below 3, then by definition you
14 would be below the standard, because that's --

15 PANEL MEMBER HAMMOND: Well, I think that's what
16 I was saying in my earlier comments. I was saying that we
17 need to make that -- I think that this document needs to
18 be very clear. Bring all those comments together in one
19 place and say the REL is three microns per cubic meter,
20 defined as this respirable by the ACGIH standards. A
21 screening can be done with PM10. If the PM10 is under 3,
22 by definition you'll be under the 3. I think that
23 should -- but this has to be in one place on the one
24 little box, one paragraph, clear.

25 CHAIRPERSON FROINES: Well, I just want to be

1 differ from the two of you a little bit. I think that the
2 issue isn't the upward bound, the way Paul is describing
3 it, because I think there are going to be lots of cases
4 where it will be above 3. Remember, that the -- you know,
5 a particle that has one micron diameter is -- a ten micron
6 diameter particle weighs a thousand times more. So a PM10
7 measurement is weighted heavily.

8 PANEL MEMBER BLANC: Oh, no, I think in the
9 same -- well, in the same sentence you can say if a PM10
10 value is above 3, it does not necessarily mean, however,
11 that you --

12 CHAIRPERSON FROINES: But the issue is you're
13 going to -- what I'm saying is you're going to find I
14 think a number of values, depending on where you measure,
15 that will be above --

16 PANEL MEMBER BLANC: Well, maybe. But they
17 haven't cited any examples.

18 SUPERVISING TOXICOLOGIST MARTY: Can I just
19 insert a little thought into the discussion about
20 exposure -- or about dealing with exposure and
21 measurement. We have not typically done that in the REL
22 documents. We've just presented basically the
23 toxicologic, epidemiologic side of things.

24 And in the Hot Spots program it's even a little
25 more complicated because most of those exposures are

1 estimated rather than measured. In talking about silica
2 sources, we have been talking about, well, they need some
3 help in estimating. And the only way you're going to get
4 help is if you actually go out and do some measurements so
5 you can tell them how to estimate. So it's a real issue.
6 I don't think we can resolve it within this document.

7 CHAIRPERSON FROINES: But I just want to -- I
8 understand what you just said and I agree with you. But I
9 also think that the reason this discussion is coming up
10 here -- and if we were dealing with hexachlorobenzene or
11 something else, it wouldn't be coming up. You know, I
12 mean it's-- we're talking silica is unfortunately a hot
13 ticket item. But, you know, without a trace on Channel 2
14 last Sunday they were talking about exposures to silica on
15 the television program. So it's not an issue that's not
16 in the public eye. And there are people who worry about
17 their kids being in sand boxes. I mean so that what we
18 have is something that has a high public interest
19 associated with it.

20 So it means that we have to be very careful on
21 this sampling question, I think. And we can defer to
22 you -- the two agencies to resolve the issue, and I'm
23 quite comfortable with that. But I think it's an issue
24 that needs to be clearly addressed, because I don't think
25 this is an abstract question by my means.

1 SUPERVISING TOXICOLOGIST MARTY: Can we have a
2 little bit of discussion in this REL document to that
3 effect?

4 CHAIRPERSON FROINES: If you want to --

5 SUPERVISING TOXICOLOGIST MARTY: I think that
6 would be really reasonable to do.

7 CHAIRPERSON FROINES: If the panel thinks that
8 would be appropriate.

9 PANEL MEMBER HAMMOND: You mean about the
10 screening that we were just talking about?

11 SUPERVISING TOXICOLOGIST MARTY: Yeah, the
12 screening and the fact that, you know, it's not standard
13 procedures to look at that size fraction for ambient
14 measures.

15 PANEL MEMBER HAMMOND: I think that would be
16 helpful to the readers.

17 CHAIRPERSON FROINES: I would argue that there is
18 sufficient agreement with the document that that would --
19 that that agreement and the other things that people have
20 suggested would not preclude our moving forward on the
21 document, but we'll take that up in a second. But I
22 think it -- I think it's in your best interests to address
23 it up front rather than saying we're simply going to
24 establish a work group. That's less satisfying to the
25 person reading the transcript who has an interest in

1 silica.

2 So let me go back then. Given the changes that
3 people have suggested, is the Panel comfortable going
4 forward with a vote on this document as such? Or do you
5 want to have Melanie come back again?

6 Paul, Katharine?

7 PANEL MEMBER HAMMOND: I think we've been pretty
8 clear about I think the very specific things. This is
9 going to -- I think this might be the first document that
10 I've been party to, and so I don't know the whole
11 procedures. But my sense is that they're pretty clear
12 things we've said; they're not major -- issues that take
13 conversation. So if there's a way that we can say, given
14 certain changes and someone checks it out on the panel,
15 then I think we could -- then we could go forward.

16 CHAIRPERSON FROINES: I don't think there's any
17 substantive disagreement. In fact I think there is
18 agreement with that.

19 PANEL MEMBER HAMMOND: Right. So I think -- to
20 my mind, then I think, you know, assuming that those
21 changes can be made, I think we could -- I would think we
22 could accept this way to do that.

23 CHAIRPERSON FROINES: Paul.

24 PANEL MEMBER BLANC: I want to give the OEHHA a
25 little bit of wiggle room here.

1 If you send an E-mail tomorrow to Churchyard and
2 if Churchyard sent you the data and if you did the
3 calculations and if they came out to be 3 again, then I
4 don't see there being an issue. But if they come out to
5 be, you know, 1 or .05 or something, is -- you know, what
6 would you do in that situation -- or if they came out to
7 be 6?

8 DR. COLLINS: I think that's always a possibility
9 with any of the chronic RELs, that better data can come
10 out.

11 PANEL MEMBER BLANC: Right.

12 DR. COLLINS: The problem we have with that
13 study, it is a cross-sectional study, so we know it's
14 going to underestimate the ultimate REL. But I doubt that
15 it's going to come out at .1 or .0 --

16 PANEL MEMBER BLANC: No, I know. I think it's
17 unlikely too. But I'm just asking. In other words the
18 two options are that we tentatively approve the document
19 presuming that the changes that -- the actions that we've
20 asked for do not lead to substantive changes. But I'd
21 like you to be able -- if you find in your review that in
22 fact the actions that we ask you to take lead to what you
23 view as potentially substantive changes, that you would
24 notify us of that. So that the wording of the resolution
25 somehow builds that into it so that you have some option.

1 I don't want you locked into -- or us locked into
2 approving a document which is in some ways substantively
3 different.

4 CHAIRPERSON FROINES: Well, I think that should
5 be almost a generic statement, that if we approve
6 something -- tentatively approve something, but in going
7 back you find substantive changes, then in fact I think
8 it's incumbent upon you to bring it back to the panel.

9 PANEL MEMBER BLANC: So I would move that the
10 panel approve the document pending the modifications
11 discussed today, and presuming that there are no
12 scientifically substantive changes to the findings.

13 CHAIRPERSON FROINES: Is there a second?

14 PANEL MEMBER LANDOLPH: Second.

15 CHAIRPERSON FROINES: Any further discussion?

16 All those in favor?

17 (Hands raised.)

18 CHAIRPERSON FROINES: Unanimous, 6 to -- 7 to 0.

19 This is a very interesting compound. I think we
20 won't hear the last of it.

21 Let's take a break.

22 (Thereupon a recess was taken.)

23 CHAIRPERSON FROINES: Mary-Ann, why don't you
24 come up and have a seat. I would have you sit next to me,
25 but there's no chair. So maybe if you could sit at the

1 table.

2 This is a real pleasure for me. Everybody in
3 this room knows that historically there has been some
4 tension between the DPR and this Panel. And so I'm really
5 happy to introduce Mary-Ann Warmerdam.

6 How do I pronounce it correctly?

7 DPR DIRECTOR WARMERDAM: Well, in the old country
8 we'd say Varmerdaum, but here it's Warmerdam.

9 CHAIRPERSON FROINES: Warmerdam. Okay.

10 Mary-Ann is the new Director of DPR. And we've
11 been exchanging E-mails. And she asked to attend a
12 meeting and introduce herself. And I think it -- we've
13 just had a very nice conversation. And I won't
14 characterize it in terms of Stan's role, but --

15 (Laughter.)

16 CHAIRPERSON FROINES: But in any case, we're
17 looking forward to working with her. And I think it's
18 going to be very positive in the future.

19 Welcome.

20 DPR DIRECTOR WARMERDAM: Well, thank you, Dr.
21 Froines. And thank you, Panel members. I did ask if I
22 could come by and just spend a moment with you to
23 introduce myself.

24 I was appointed Director of DPR about a month
25 ago -- well, close to six weeks ago now, have been on the

1 job a month. So there's much that I don't know about the
2 Department's functions. But I'm absolutely delighted to
3 be with the Department.

4 And I want to start out by thanking you all for
5 spending your time doing the scientific work. I am not a
6 scientist by training. I am a policy person. I've spent
7 most of my professional career working on either
8 agricultural or water, natural resource policy. And so
9 coming to a panel like this is really quite illuminating,
10 and I do appreciate the work that you've done.

11 As Dr. Froines said, we've had a sometimes
12 checkered history, "we" being DPR, with the Panel. But
13 this Governor has been very clear in his direction to --
14 at least to me, and that we want to have transparency, we
15 want to have economic growth, and we want to have
16 environmental improvements. And to the extent that we can
17 effectively do that together, I look forward to working
18 with you all in reaching those goals on behalf of the
19 Governor.

20 And with that, if there are any questions any of
21 the panelists would like to ask. Otherwise I'll leave you
22 to your next discussion item.

23 CHAIRPERSON FROINES: Thank you.

24 Any questions?

25 DPR DIRECTOR WARMERDAM: Thank you very much.

1 PANEL MEMBER HAMMOND: Thank you for coming.

2 DPR DIRECTOR WARMERDAM: You're welcome.

3 CHAIRPERSON FROINES: Okay. We are trying to
4 figure out what we're going to do about lunch.

5 PANEL MEMBER GLANTZ: I think we should work
6 through lunch.

7 CHAIRPERSON FROINES: That would take us to about
8 2 o'clock. Is the panel --

9 PANEL MEMBER GLANTZ: No, I mean get lunch and
10 eat while we're talking.

11 CHAIRPERSON FROINES: Is it possible, Peter? Can
12 we -- is the Panel agreeable to having lunch brought in
13 and continuing till 2?

14 Any problems?

15 Okay. We're off and running.

16 My assumption is that we're going to spend most
17 of the next three hours going through the presentations.
18 And then in January 6th, we will have a full panel
19 discussion and hopefully we can get through the document
20 at that time.

21 PANEL MEMBER BLANC: Well, the only other agenda
22 item -- and this is going to be a question more for
23 Peter -- is whether or not there should be some discussion
24 here of future dates that would narrow down the blocks. I
25 find it difficult to respond to the last date request,

1 because basically it was like "Tell me your availability
2 for the rest of the year." And that's somewhat tedious.
3 I would rather respond to, you know, "Of the last two
4 weeks of," you know, "March when are you available?" Or
5 something a little bit more focused. So I think having
6 some time set in the meeting to talk about when it is you
7 want to meet after the January meeting would be helpful to
8 me.

9 CHAIRPERSON FROINES: Well, let me ask the
10 question then a little differently than you just said it.

11 We are meeting here November 30th and we have a
12 meeting January 6. So it's a little bit more than a month
13 difference between the meetings.

14 Given people's schedules, how long after January
15 6th would you be comfortable holding a meeting? Do you
16 want a month? Do you want two months? What's your --

17 PANEL MEMBER GLANTZ: Well, I think it sort of
18 depends on what happens at the January 6th meeting,
19 because I'd like to not have this document drag on for a
20 really long time. So what you might want to do is
21 schedule -- I mean the other thing is what else is on the
22 agenda?

23 CHAIRPERSON FROINES: The other item on the
24 agenda --

25 PANEL MEMBER GLANTZ: I mean for the future.

1 CHAIRPERSON FROINES: And Mary-Ann I think left.
2 But we have sulfurofluoride coming up.

3 PANEL MEMBER GLANTZ: And when will that that be
4 ready?

5 CHAIRPERSON FROINES: It's ready.

6 PANEL MEMBER BYUS: No, no, no, not exactly.

7 CHAIRPERSON FROINES: Close.

8 PANEL MEMBER BYUS: I'm having them rewrite part
9 of it. There's been some additions which they've just got
10 back to me.

11 CHAIRPERSON FROINES: Well, what's your guess?

12 PANEL MEMBER BYUS: It should be ready in
13 January, hopefully. It depends. I haven't actually read
14 all that they have written.

15 CHAIRPERSON FROINES: So let's assume January.
16 So let's assume that it's going to be available after the
17 first of the year.

18 PANEL MEMBER BYUS: Right.

19 CHAIRPERSON FROINES: Just as a touch point.

20 So, Stan, I agree with you that we don't want
21 this document to -- we want to move this document along.
22 At the same time, this is a major document, and we want to
23 have a very clear record, a thorough review and analysis.
24 And so I think we have to take the time that it's going to
25 take.

1 PANEL MEMBER GLANTZ: No, I agree with that.
2 It's just if the -- especially if you're saying that most
3 of the meeting today is going to be the presentation
4 rather than discussion, I mean I would -- it might be that
5 the thing to do is to try to schedule another meeting
6 at -- I mean we may finish it with the January 6th. I
7 would worry that we might not.

8 So then I would suggest, especially if there's
9 another document coming down the pipe, that you schedule a
10 couple of more meetings like in about a monthly interval
11 or something.

12 PANEL MEMBER BLANC: I would sort of take a
13 middle ground. And what I would suggest --

14 PANEL MEMBER GLANTZ: You can always cancel them.

15 PANEL MEMBER BLANC: Well, even taking that into
16 account, what I would say is that it would probably be
17 helpful for us to schedule an early March meeting, which
18 if we don't need, we can cancel. I don't think I would be
19 very happy about a January and a February meeting.

20 CHAIRPERSON FROINES: Can I ask one question
21 about that?

22 I'm going to China for three weeks because we
23 have a lung cancer project.

24 PANEL MEMBER BLANC: And when are you leaving?

25 CHAIRPERSON FROINES: About the second week in

1 March. So I'd like to -- if we could do it, I'd like
2 either the last week of February or the first week in
3 March.

4 PANEL MEMBER BLANC: First week in March would be
5 I think a good compromise, wouldn't it?

6 PANEL MEMBER GLANTZ: Well, I think -- why don't
7 we say -- why don't we agree to the last week of February
8 or the first week of March and see what date works for the
9 most people.

10 CHAIRPERSON FROINES: Charlie, are you okay?

11 PANEL MEMBER PLOPPER: Yes.

12 CHAIRPERSON FROINES: Craig?

13 PANEL MEMBER BYUS: (Nods head.)

14 PANEL MEMBER GLANTZ: Because we are going to
15 have -- in addition to finishing the ETS document, we're
16 going to have this other one. And it's very hard for me
17 to believe we could get through two things at one meeting
18 on January 6th and do it well.

19 CHAIRPERSON FROINES: I had a meeting with
20 Secretary Tamminen about a month ago. And one of the
21 things that we discussed was how's the panel functioning.
22 And Secretary Tamminen is no longer Secretary of CalEPA.
23 He's now in the Governor's office. But the one thing that
24 we agreed to was that we are going to, at some point next
25 year -- and I say next year, so nobody needs to be

1 worried -- is have a half day or a day long workshop on
2 what are the kinds of chemicals that should be coming
3 before this Panel in the long term. So it's a long-term
4 planning meeting, not a short-term planning meeting. And
5 it doesn't have to occur until December 2005. But it's
6 one of the things that we'll have on our agenda for the
7 future.

8 PANEL MEMBER BLANC: Well, then rather than
9 belabor this more now, Peter, can you follow up for this
10 meeting, circulate it E-mail, but focused on the last week
11 in February, first week in March?

12 MR. MATTHEWS: I will.

13 CHAIRPERSON FROINES: We'll work it out.

14 Kathy and I have a conflict in the first week in
15 March.

16 PANEL MEMBER LANDOLPH: I'll be gone 28th of
17 February 1st and 2nd of March.

18 CHAIRPERSON FROINES: Yeah. Paul was making that
19 suggestion so we would avoid exactly what we're getting
20 into. So let's not get into individual schedules.

21 PANEL MEMBER BLANC: Plus we have tow people that
22 aren't here today, so we'd need to here from them.

23 CHAIRPERSON FROINES: And I think today one of
24 the reasons I'm hoping that we spend most of the time on
25 presentation is I think it's very, very important to have

1 a fully prepared Gary Friedman as our epidemiologist for
2 the January meeting. So that the discussion on various
3 epidemiologic studies I think is -- I'm going to work with
4 him, and I think OEHHA can work with him, to make sure
5 that over the holidays and everything he's well prepared
6 for that January 6th meeting.

7 PANEL MEMBER GLANTZ: Yeah, just one last thing.
8 I just was looking at Joe's calendar. And the last --
9 february 28th is a Monday. So just to be precise, I would
10 say that you try to get a meeting scheduled between the
11 21st of February and the 4th of March or maybe the 11th of
12 March.

13 CHAIRPERSON FROINES: We'll move ahead, unless --
14 Paul is looking at his calendar -- and says those don't
15 work.

16 PANEL MEMBER BLANC: No, no, no. I'm fine.

17 CHAIRPERSON FROINES: Okay. Jim, let's go.

18 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
19 Very good.

20 Well, good morning to Dr. Froines and the rest of
21 the Panel. Appreciate your consideration of our report
22 this morning.

23 My name is Jim Aguila. I'm the Manager of the
24 Substance Evaluation Section within the Air Resources
25 Board. And our group was responsible for developing the

1 exposure assessment, and will also be the primary group
2 that takes us through the legal rulemaking process for
3 eventually identifying environmental tobacco smoke as a
4 toxic air contaminant.

5 This morning's strategy, what we intend to do is
6 tag team with OEHHA in our presentation today. And
7 actually one of my staff will be giving our presentation
8 on the exposure assessment. And then we'll turn it over
9 OEHHA for their part.

10 So with that, I'll go ahead and introduce Robert.

11 CHAIRPERSON FROINES: Can everybody see okay? It
12 seems to me a little light. And should we move this over?
13 How are you?

14 PANEL MEMBER GLANTZ: Okay. It's fine.

15 PANEL MEMBER BLANC: If your okay, then we're
16 okay.

17 MR. KRIEGER: Thank you, Jim.

18 As Jim mentioned, my name's Robert Krieger. I'm
19 staff lead for the proposed identification of ETS as a
20 TAC.

21 (Thereupon an overhead presentation was
22 Presented as follows.)

23 MR. KRIEGER: Today we'll be providing you with a
24 summary of the SRP version of the draft report proposed
25 identification of the environmental tobacco smoke as a

1 toxic air contaminant.

2 --o0o--

3 MR. KRIEGER: Developed by the Air Resources
4 Board and the Office of --

5 CHAIRPERSON FROINES: Just for Dr. Plopper.
6 People -- most of this discussion will occur at the
7 January 6th meeting. But keep in mind that people always
8 break into to the presentation for questions. So there's
9 no problem.

10 PANEL MEMBER BLANC: Just like he's doing now.

11 MR. KRIEGER: Thank you. Good example.

12 The information presented in this report will
13 serve as the basis for its identification as a toxic air
14 contaminant.

15 I will be giving an overview of the ARB's
16 exposure assessment evaluation, followed by Dr. Melanie
17 Marty of the Office of Environmental Health Hazard
18 Assessment, who will provide a presentation on OEHHA's
19 health assessment report.

20 Included in each presentation will be a summary
21 of comments and responses to these comments we received on
22 the respective parts during the public comment period
23 earlier this year on the initial draft report dated
24 December 2003.

25 Our presentation will conclude with a slide

1 describing the next steps of the process.

2 --o0o--

3 MR. KRIEGER: State law requires that ARB assess
4 exposures to a substance suspected to cause adverse public
5 health effects for people in California. The law also
6 requires the OEHHA to evaluate health effects of the
7 substance and to determine if the threshold of the
8 significant adverse health effects exists for that
9 substance.

10 SB 25 established the Children's Health
11 Protection Act of 2001. Specifically for air toxic
12 identification it requires that health risk assessments
13 include an analysis of children's exposure and health
14 impacts from each substance. We have addressed these
15 requirements in the public report.

16 Next slide.

17 --o0o--

18 MR. KRIEGER: This slide shows the definition --
19 legal definition of a toxic air contaminant, which is: "A
20 toxic air contaminant is defined in California law as an
21 air pollutant which may cause or contribute to an increase
22 in mortality or in serious illness or which may pose a
23 present or potential hazard to human health."

24 --o0o--

25 MR. KRIEGER: This chart shows the toxic air

1 contaminant identification process we follow to ensure
2 that any regulation we propose will be based on good
3 science. The process provides for publicly review and
4 complies with all the applicable administrative
5 requirements.

6 Initially, the ARB undergoes a process to
7 prioritize substances of concern to determine if they
8 should be selected for evaluation.

9 Once we have entered a substance into the
10 identification process, we work with OEHHA to develop a
11 report which will serve as the basis for the
12 identification. OEHHA develops the health effects portion
13 of the report, while ARB develops the exposure data. The
14 report then undergoes public review, with a public
15 workshop held generally towards the end of the comment
16 period.

17 The Scientific Review Panel on toxic air
18 contaminants then conducts peer review of the report and
19 provides its findings to the ARB. At that point, the ARB
20 initiates the rulemaking process with the public release
21 of the staff report, which contains the staff's proposal
22 to list ETS as a toxic air contaminant. The public is
23 given a 45-day comment period on the initial statement of
24 reasons. And the process culminates with a board hearing
25 to consider identifying by regulation ETS as a TAC.

1 --o0o--

2 MR. KRIEGER: This slide presents a chronology of
3 ETS-related work that brings us to where we are today.

4 In February of 1992 a collaborative agreement
5 between the ARB and OEHHA was reached to initiate a report
6 on the health effects of ETS, as requested by the
7 Scientific Review Panel.

8 The final draft of this report was reviewed and
9 approved by SRP in 1997. Subsequently the National Cancer
10 Institute recognized the importance of the report and
11 incorporated it into their smoking and tobacco controlled
12 monograph series in 1999.

13 In June 2001 ETS was formally entered into the
14 toxic air contaminant identification process, given its
15 significant health risks to the public, particularly
16 children.

17 In December of last year, the draft ETS
18 identification report was released for public comment.

19 In March of this year, a public workshop was held
20 to discuss the report.

21 We responded to public comments on -- report this
22 past October.

23 --o0o--

24 MR. KRIEGER: Now on to our Part A, Exposure
25 Assessment.

1 --o0o--

2 MR. KRIEGER: With that background I'll now
3 review the Part A, Exposure Assessment.

4 The exposure assessment meant incorporates
5 information from Chapter 2 of the 1997 OEHHA report.
6 However, much of our exposure assessment was information
7 that was not presented in the original OEHHA report.

8 As with other identification reports, our report
9 addresses the areas required by law. They include
10 information on a substance's chemical and physical
11 characteristics, sources and emissions, a measure of an
12 estimate of ambient concentrations, indoor and total
13 exposure, children's exposure, and a substance's
14 persistence in the atmosphere.

15 --o0o--

16 MR. KRIEGER: ETS is well established that it is
17 a complex mixture of gases and fine particle emitted
18 primarily by the burning of tobacco products and from
19 smoke exhaled by the smoker. Other minor contributors are
20 from the smoke that escapes while the smoker inhales and
21 some vapor phase-related compounds that diffuse from the
22 tobacco product.

23 Many of the substances found in ETS have known
24 adverse health effects. For directly emitted side-stream
25 smoke and mainstream smoke, most ETS particles can range

1 in size from .01 to 1 micrometer.

2 --o0o--

3 MR. KRIEGER: Since smokers are the origin of ETS
4 emissions, smoking prevalence provides a helpful
5 indication of how ETS exposure is generated and by whom.
6 According to the California tobacco survey data collected
7 by the California Department of Health Services, smoking
8 prevalence among adults and adolescence has decreased over
9 the past decade.

10 Since the passage of Proposition 99 in 1988,
11 adult per capita cigarette consumption decreased by over
12 16 percent in California. In 2002, California adult
13 smoking prevalence was 16 percent and lower than the rest
14 of the nation. Credit here should be given to the
15 California anti-smoking laws and programs that help with
16 smoking cessation.

17 In 2001 the California Students Tobacco Survey
18 was adopted by the Department of Health Services as a more
19 accurate survey to measure adolescent smoking behavior.
20 The CSTS utilizes in-school surveys, which are expected to
21 be much more accurate as opposed to the random phone calls
22 performed under the original CTS.

23 The Latest results of the survey showed 16
24 percent of California adolescent population smokes.

25 --o0o--

1 MR. KRIEGER: This slide shows ARB's estimated
2 total statewide emissions for some of the pollutants
3 commonly associated with ETS. The basic calculation is
4 straightforward: Emission factors times the products
5 consumed. We repeated the calculation for both cigarettes
6 and cigars and added the results to obtain the total.

7 Sales tax information from the Board of
8 Equalization, emission factor studies, and the California
9 tobacco survey were used to estimate statewide and
10 county-by-county emission estimates.

11 Staff then adjusted -- had applied an adjustment
12 factor to account for the fact that smokers generally burn
13 about 90 percent of tobacco column.

14 --o0o--

15 MR. KRIEGER: How do we measure ETS exposure?
16 There are a number of components associated with
17 determining ETS exposure due to its complex mixer such as
18 the ability to determine the appropriate marker that
19 represents ETS as a whole. Several components of ETS have
20 been used as markers: Nicotine, solanesol, 3-EP,
21 iso-anteisoalkanes, PAHs, and RSP.

22 Nicotine has been the most widely used marker
23 because its unique to tobacco smoke.

24 --o0o--

25 MR. KRIEGER: Two published studies measured

1 outdoor concentrations of ETS:

2 Rogge in his study measured fine particles of ETS
3 in a range from .28 to .36 micrograms per cubic meter.

4 Eisner used passive benchmark to measure nicotine
5 concentrations over a 7-day period. The results show an
6 average concentration level of .025 micrograms per cubic
7 meter of nicotine.

8 To fill the gap in California's ETS ambient
9 exposures ARB also collected data through ambient ETS air
10 monitoring study. ARB monitored nicotine concentrations
11 at several outdoor smoking areas in California. The
12 results showed a range of concentrations from .01 to 3.1
13 micrograms per cubic meter for an 8-hour period and .039
14 to 4.6 microgram per cubic meter for a 1-our period.

15 PANEL MEMBER BLANC: The Eisner study is not a
16 pure outdoor nicotine study and you can't use it in the
17 way that you're citing it here.

18 MR. KRIEGER: Is that --

19 PANEL MEMBER BLANC: It's a 7-day integrated
20 indoor/outdoor, to wherever people --

21 MR. KRIEGER: You're correct. It is an
22 integrated study. They do provide an outdoor number, but
23 it is integrated.

24 PANEL MEMBER BLANC: It's not an outdoor by
25 nature, but there are outdoor hours of self-reported

1 exposure. And you could probably take the average outdoor
2 hours as a percentage of total hours and multiply it.
3 Although I think that that would presume that the
4 concentration was the same, which you can't do. So I
5 don't think you can cite that here for the purposes that
6 you seem to be trying to site it, which is as a measure of
7 outdoor --

8 PANEL MEMBER HAMMOND: I think there was a part
9 of that -- I think -- I agree with that part. But I think
10 there's a part of that study where some of the people in
11 the study were only exposed outdoors. And I didn't --

12 PANEL MEMBER BLANC: Yes. But I don't --

13 PANEL MEMBER HAMMOND: They had no indoor
14 exposure.

15 PANEL MEMBER BLANC: Yeah. But I don't know if
16 there was a separate calculation done in that study. You
17 can look.

18 MR. KRIEGER: I believe there was a separate
19 calculation in there. But I can --

20 PANEL MEMBER HAMMOND: And this may be that
21 number.

22 PANEL MEMBER BLANC: And is that what you're
23 using?

24 MR. KRIEGER: That was the one we were using the
25 separate calculation for that. But I know it was an

1 integrated study and I --

2 PANEL MEMBER HAMMOND: I thought some people
3 reported it only exposures that --

4 PANEL MEMBER BLANC: Okay. If that's true,
5 that's okay then. I just want to make sure that --

6 MR. KRIEGER: I mean there --

7 PANEL MEMBER BLANC: Just double check if that's
8 what you did.

9 MR. KRIEGER: Well, we'll double check that and
10 make sure. But I believe that was the one. That was the
11 number that we used for the study. But like I said,
12 there's not too many outdoor --

13 PANEL MEMBER BLANC: No, I understand.

14 MR. KRIEGER: Oh, and our last number -- bullet
15 there, our last was to provide a perspective on general
16 exposure. And we did the -- the ARB staff estimated
17 statewide annual average annual concentration for ETS
18 particulate and nicotine to be .02 micrograms per cubic
19 meter and .0025 micrograms per cubic meter, respectively.

20 --o0o--

21 CHAIRPERSON FROINES: How was that arrived at?

22 MR. KRIEGER: That was taken into account for
23 emissions inventory and emission factors for ETS from
24 cigarettes themselves. So we merely did a simple
25 calculation of it: What's the inventory of ETS

1 particulate in California and ETS nicotine in California,
2 taking into account the number of cigarettes smoked in
3 California, the number of cigars smoked in California as
4 well? And the fine PM inventory in California and taking
5 a percentage of that.

6 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:

7 Actually --

8 PANEL MEMBER HAMMOND: But is there an underlying
9 assumption then that the ETS is equally distributed
10 throughout the state?

11 MR. KRIEGER: Yes, there's a big assumption
12 there.

13 PANEL MEMBER HAMMOND: And that's probably an
14 inaccurate assumption.

15 PANEL MEMBER BLANC: And then how did you arrive
16 at how much of the cigarette consumption was consumed
17 outdoors?

18 MR. KRIEGER: We're assuming that all of the
19 cigarettes consumed indoors makes it outdoors. We have a
20 number of assumptions here that we used.

21 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:

22 Yeah, it was a total estimate.

23 MR. KRIEGER: It was a total estimate.

24 CHAIRPERSON FROINES: That's a very questionable
25 estimate.

1 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
2 Basically what we wanted to do is to provide some
3 perspective in the case where you would have concentrated
4 smokers and have -- is it possible to estimate some kind
5 of a background level? And we had -- as Robert mentioned,
6 we had PM10 emissions inventory data, and then we used
7 that with emission factor studies to correlate the RSP
8 from tobacco smoke, and were able to determine these
9 background numbers based on the existing inventory PM10.

10 CHAIRPERSON FROINES: But if the -- if much of
11 the smoking that you're actually estimating comes from
12 indoor smoking -- tobacco smoke is sticky stuff. And so
13 whether or not that ever has a slightest change to occur
14 outdoors, but that could be a very misleading estimate.

15 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
16 Yeah, that's one of our underlying assumptions, is that
17 the smoking occurs outside.

18 PANEL MEMBER BLANC: But don't you know from
19 other survey information how many cigarettes people smoke
20 outside? I mean the California Tobacco Survey is quite
21 detailed.

22 Stan, do you know if they --

23 PANEL MEMBER GLANTZ: I don't remember if they
24 asked the question, "Do you smoke inside or outside?" But
25 I think that there are probably good data in the

1 literature on that.

2 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:

3 Yeah, we found literature to indicate that most of the
4 smoking, you know, occurs outside. But we didn't have an
5 exact number or percent.

6 PANEL MEMBER GLANTZ: In California that may be
7 actually getting true because of all the smoke. I don't
8 know if that would be true nationally. But in California
9 most smoke -- you know, a lot of the smoking is now
10 outside.

11 PANEL MEMBER BLANC: Well, I think it would be
12 worth incorporating some fractional discount in your
13 number that says, "Okay, we are going to conservatively
14 assume that on average," you know, one out of four
15 cigarettes that are smoked are smoked outside. Or here's
16 the range if we assume that it's one out of four and here
17 is if it's three out of four --

18 MR. KRIEGER: Okay.

19 PANEL MEMBER BLANC: -- or something. Because
20 otherwise the face validity of the exercise seems too
21 dubious.

22 CHAIRPERSON FROINES: The other problem is that
23 the -- it's not clear what you want to use a number like
24 that for. And that number will be get quoted everywhere
25 in every newspaper when it covers this kind of issue. And

1 so there will be an assumption that there's some
2 significant validity to the number. And so we just want
3 to be careful not to give misleading information for which
4 we don't really have a reason for that.

5 PANEL MEMBER HAMMOND: Well, and I'm equally
6 concerned or maybe even more so about the geographic
7 distribution. In other words, almost certainly there's
8 more emitted where there are more people living. And
9 there's going to be more -- so that concentration of that
10 area will be higher and the exposures of people who are
11 outdoors in that area where most of the population is will
12 be higher.

13 So for two ways that underestimates exposure to
14 spread it through the entire study.

15 MR. KRIEGER: Those are good comments.

16 Okay. Now, on Indoor study --

17 PANEL MEMBER GLANTZ: Just one other comment on
18 this.

19 You know, the way I sort of think about the
20 outdoor exposures is more like a hot spot rather than a
21 broad ambient exposure. And so you might want to be
22 thinking about it in those terms too.

23 MR. KRIEGER: Yeah. And --

24 PANEL MEMBER GLANTZ: And that certainly would
25 fit with the way you did this -- you know, the studies

1 you're probably going to talk about that you guys did,
2 which are in the appendix Part A, I mean those are really
3 kind of hot spot studies rather than broad ambient
4 studies.

5 MR. KRIEGER: And I think that's -- yeah, that's
6 a good point. I think Dr. Glantz has a good point. And I
7 know we speak on the next proceeding slides, where we
8 focus our attention on the scenarios that we've done,
9 which incorporates the hot spot exposure. Because ETS is
10 localized and that's more of a hot spot issue versus the
11 statewide population layer, any kind of estimate that we
12 have.

13 --o0o--

14 MR. KRIEGER: Several studies that measured ETS
15 concentrations indoors, in different environments using
16 primarily nicotine and RSP as markers for ETS, an
17 exposure. Indoor concentrations of nicotine are estimated
18 to range from .5 to 6 microgram per cubic meter in the
19 home environment, and 2.2 to 8 micrograms per cubic meter
20 in offices or public buildings where smoking is allowed,
21 and less than 1 microgram per cubic meter in public
22 buildings where smoking is prohibited.

23 As also indicated, certain work places such as
24 free-standing bars in betting establishments that do not
25 comply with California's work place smoking ban would

1 likely have higher levels of ETS.

2 --o0o--

3 MR. KRIEGER: As we talked about just briefly, a
4 scenario-based approach is used to characterize the range
5 of the public's exposure to ETS in this report. We
6 believe this approach provides more informative estimates
7 of public exposure to ETS than population-weighted outdoor
8 ambient exposures calculated for previous TAC exposure
9 assessments. This approach takes into consideration that
10 cigars and cigarettes, the primary source of ETS, are
11 small sources that emit pollutants near people and that
12 these exposures are localized.

13 The scenario-based exposure method uses the
14 results from ARB's nicotine air monitoring study,
15 available indoor ETS concentration data, and activity
16 patterns to estimate exposures under different conditions
17 for various segments of our population.

18 The results of the different scenarios indicate
19 that exposures to ETS can vary in many different
20 situations. Daily exposures for individuals living in
21 nonsmoking homes and having only brief encounters with
22 smokers are estimated to be less than 1 microgram per
23 cubic meter. Individuals living in homes with indoor
24 smokers and experiencing other ETS exposures throughout
25 the day may result in higher exposures of about 3

1 micrograms per cubic meter. For some of the population
2 outdoor smoking can contribute from virtually 0 to 100
3 percent of an individual's exposure to ETS.

4 --o0o--

5 MR. KRIEGER: Another method for estimating human
6 exposures to ETS is through the use of biomarkers.
7 Cotinine, the major metabolite of nicotine, has emerged
8 over the past 20 years as a widely used biological marker
9 for most field exposure studies. Cotinine is sensitive
10 enough that its concentration can reliably distinguish
11 between non-ETS exposed persons and ETS exposed
12 non-smokers with low, moderate, and high levels of
13 exposure.

14 Nicotine in hair is an emerging biomarker that
15 may be as effective as cotinine in predicting levels of
16 ETS exposure.

17 Other biomarkers of exposure such as DNA and
18 protein adducts of ETS link ETS exposure directly to
19 carcinogenic metabolites.

20 PANEL MEMBER BLANC: Doesn't that list also need
21 to include some of the other nicotine metabolites that
22 people like -- which we're starting to look at? I mean
23 this is just a table you're presenting. But in the
24 document, do you at least allude to that even if they're
25 not ready for prime time?

1 DR. WINDER: Well, there is some discussion of
2 other biomarkers and their relative effectiveness compared
3 to the cotinine in nicotine. And the conclusion being
4 that these two at this point in time are the best we have.

5 PANEL MEMBER HAMMOND: I think the purpose of
6 these biomarkers is to evaluate the exposure of a
7 population. And to that degree, it has to be established
8 by the markers as opposed to the research level. Is that
9 correct -- a correct interpretation?

10 PANEL MEMBER BLANC: And you feel you're clear
11 enough about that.

12 And there's a sufficient discussion of the
13 shortcomings of -- the timeframe shortcomings of cotinine,
14 or limitations in terms of it being a fairly recent ETS
15 exposure marker and how as we start to look at populations
16 with intermittent exposures, which only occur in ambient
17 hot spot areas, a urinary cotinine measure is likely to be
18 a poor assessment tool in that regard as compared to more
19 integrated cumulative measures. In other words, even if
20 I -- if I was exposed heavily to ETS every Friday, and you
21 sampled my urinary cotinine every Wednesday, you would
22 have -- you would think I wasn't exposed at all. But if
23 you had a more integrated measure, you would catch the
24 fact that every Friday I go to Bingo and have this heavy
25 exposure.

1 I mean do you feel that that's adequately
2 discussed as a limitation in your --

3 DR. WINDER: Well, there's a discussion in
4 several places in the document regarding the time period
5 over which both serum and urinary codeines are appropriate
6 and the limitations with respect to short-term exposure.

7 Your suggestion with an integrated marker is a
8 point well taken. But it's not something that's occurred
9 at least in many studies.

10 PANEL MEMBER BLANC: But it does tend to mean
11 that some of the estimates you have will be underestimates
12 of precisely the kind of exposure scenarios which are most
13 important to the document, and that all the bias is
14 towards underestimation. Isn't that correct? Or am I --
15 is that a fair -- to the extent that someone's exposure is
16 regular indoor. I live with a smoker or I work with
17 smoker in an indoor environment, the latter being now
18 taken largely out of the mix in California. Then for
19 those kinds of populations cotinine is not such a bad
20 marker because your sampling issues are -- the day-to-day
21 variability is, although present, is not huge.

22 But to the extent that someone's exposure is
23 predominantly ambient and, by definition, predominantly
24 hot spot with peaks and valleys that are intermittent,
25 then the cotinine tool becomes more and more prone to

1 missing the exposure and, therefore, falsely categorizing
2 somebody as underexposed, and will only categorize them as
3 exposed when you catch them the day after one of these
4 events.

5 MR. KRIEGER: Well, that's a good comment, Dr.
6 Blanc. We'll certainly go back and take a look at what we
7 have in the report and revise that to our -- and
8 strengthen that section to talk about the variability and
9 the sampling.

10 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
11 I think we should add some text to qualify basically the
12 point you're making, Dr. Blanc.

13 CHAIRPERSON FROINES: Can I make one comment.

14 This last statement of DNA and protein adducts
15 less useful in quantifying exposure. Is there going to be
16 a discussion presumably by OEHHA at some point about the
17 biomarker issue or --

18 PANEL MEMBER HAMMOND: You mean as a risk
19 estimator as opposed to --

20 CHAIRPERSON FROINES: Well, you see, the trouble
21 with DNA adducts is that people use them for various
22 reasons. And I think that often there's a lot of
23 confusion specifically with respect to timing, that if you
24 measure DNA adducts, you're measuring -- in fact the BAP,
25 for example, is bound with a DNA at that particular

1 timeframe. And so it's -- so people use them because they
2 think they have mechanistic significance. They use them
3 as potential for linkages with epidemiology and they --
4 but in fact what it is is a measure of exposure. And we
5 need to be sure we're clear on some of these studies
6 that -- because there are a lot of studies that have
7 looked at APB and BAP and what have you.

8 So at some point during this process, we need to
9 have a discussion about the nature of biomarkers I think.

10 SUPERVISING TOXICOLOGIST MARTY: This is Melanie
11 Marty.

12 There are a few studies that looked at DNA
13 adducts and tried to correlate that with, for example,
14 breast cancer risk. And I think most of those studies the
15 authors themselves recognized the difficulty of trying to
16 make those types of correlations, because of differences
17 in individual variability and metabolizing the carcinogen
18 to the DNA adducting ultimate carcinogen and just kinetic
19 issues. So there's some discussion about that.

20 CHAIRPERSON FROINES: Well, there's a temporal
21 issue --

22 SUPERVISING TOXICOLOGIST MARTY: Right, the
23 temporal issue.

24 CHAIRPERSON FROINES: You know, a latency issue.

25 Are we going to talk about that at some point?

1 SUPERVISING TOXICOLOGIST MARTY: Just a little
2 bit when we talk about the breast cancer. But there's
3 more discussion in the document.

4 CHAIRPERSON FROINES: Yeah, I know there's
5 discussion in the document. And that's what primed me to
6 raise this, because I think there's -- there is some
7 misunderstanding about the nature of these.

8 PANEL MEMBER BYUS: It's exposure versus
9 mechanism is really the question with the adducts.

10 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
11 That's right.

12 --o0o--

13 MR. KRIEGER: The constituents of ETS undergo
14 independent atmospheric reactions. In general, gaseous
15 chemicals of ETS can react in the atmosphere with other
16 pollutants and sunlight to form new chemical species.

17 Nicotine, the principal alkaloid in tobacco,
18 which is most commonly found in the gas -- environment.
19 In the ambient air nicotine may react with hydroxyl
20 radicals to have a half life of approximately one day.
21 ETS particles are subject to deposition and atmosphere
22 transformation of species adsorbed to the particles. One
23 chamber study showed that these particles can persist of
24 up to five hours.

25 CHAIRPERSON FROINES: But there's the other

1 category that we've been looking at in terms of air
2 pollution and, that is, when those hot vapors come out of
3 the cigarette, don't you have also some volatile particle
4 formation as well?

5 PANEL MEMBER HAMMOND: There's evaporation.

6 CHAIRPERSON FROINES: Well, there's evaporation,
7 but there's also --

8 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
9 There's a number of things.

10 CHAIRPERSON FROINES: -- in the wintertime you're
11 going to get condensation and you're going to form
12 particles. We see that -- that's what happens when things
13 come out of the tailpipe. They form particles by
14 condensing.

15 MR. KRIEGER: Yes.

16 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
17 Like aerosols.

18 CHAIRPERSON FROINES: What?

19 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
20 Forming aerosols or --

21 CHAIRPERSON FROINES: Yeah. Vapors can evaporate
22 and vapors can condense. And both things happen. And so
23 you're going to have some particle formation as -- and
24 they're going to be very volatile particles relative to
25 what Kathy's talking about which is the evaporation of

1 organics and things off the particles.

2 So my sense, and I don't know the literature on
3 this, is that you may have some particle formation that
4 also occurs.

5 PANEL MEMBER BLANC: I fear to ask this question
6 in front of an industrial hygienist.

7 When you say particle here, do you mean both
8 solid particulates and liquid aerosols? Is that what you
9 mean by particulate here?

10 MR. KRIEGER: Well, from my understanding that's
11 what the literature says.

12 PANEL MEMBER BLANC: And that's your intent?

13 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
14 Yeah, we recognized that there are components that are
15 being formed from VOC's. Likewise, there's also
16 particulates that sublimate mate too and --

17 MR. KRIEGER: And we also recognize the vapor --
18 you know, the vapors coming off can form particulates,
19 especially when it cools, any particular temperature
20 really. But we recognize that too as well. And there are
21 some literature that shows that as well.

22 PANEL MEMBER HAMMOND: I think it -- it's pretty
23 complex. I mean I don't know whether -- I think it's
24 important either not to try to attempt to do this or to do
25 a really thorough review. I think to do it superficially

1 would be a mistake, because there's also a lot of
2 literature about volatilization, especially as there's
3 less concentration and particle size is getting smaller,
4 rather -- you know, especially I would think outdoors.

5 But I don't know. Is that something you want to
6 go into in -- I think you'd need to choose whether to go
7 in-depth or to just to -- but I wouldn't do it
8 superficially.

9 But then, again, they can react with other things
10 that are in the atmosphere, that aren't in a house maybe,
11 but they're outdoors.

12 PANEL MEMBER BLANC: Well, clearly the ARB has a
13 lot of experience in talking about engine emissions. Is
14 there some corollary here that you could summarize briefly
15 that would put it in that context? Since part of what the
16 exposure document is trying to do is put ETS on the same
17 footing of other airborne pollutants, right?

18 MR. KRIEGER: You're right, yeah.

19 PANEL MEMBER BLANC: And the model of having to
20 deal with non-stationary internal combustion emission
21 mixes is not so very different, is it?

22 MR. KRIEGER: No, it's not. And, for instance,
23 diesel exhaust, you know, a complex mixture, it's the same
24 sort of deal. I mean you have different sources obviously
25 in different locations. It's not as localized. But you

1 still have the complex mix coming out of the tailpipe and
2 eventually ending up into the atmosphere. And you're
3 having different reaction products over the vapor phase
4 and the particle phase, all those different reactions.
5 And we addressed it in diesel exhaust, I know. We briefly
6 mentioned on the gaseous components and the particle
7 components just like we did here. We didn't go in-depth.

8 I mean we could go in-depth for every, you know,
9 reaction and the different reactions that happen in the
10 atmosphere with the different radicals and reactions
11 within themselves, the organics playing with each other to
12 form particles.

13 We didn't go in depth in this. And certainly we
14 could. But we felt for this identification report -- the
15 law specifically tells us to address this comment. But as
16 far as the details with all the minutia, we didn't -- we
17 chose not to do this. Because, like Dr. Hammond
18 suggested, there's a number and it can -- it's
19 overwhelming at times for the amount of information.

20 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
21 Would it make sense to expand the discussion of
22 particulate component and reaction to include aerosols --
23 aerosol component reactions? That seems like it would be
24 more comprehensive, to be more clear in our report that
25 we're actually talking about both, not just VOC related

1 but the solid particulates too.

2 CHAIRPERSON FROINES: Well, I should say that we
3 have just published about five papers on particle
4 formation from vapors that have never been published
5 before. And so the question is -- and we find very
6 different particles formed by condensation of vapors. And
7 so we can give you those papers. And then you can think
8 about whether or not this has any relevance to
9 environmental tobacco smoke.

10 But this isn't -- this is not in the literature.
11 This is new findings. For example, we've just done a
12 major study at the Caldecott Tunnel, and so on and so
13 forth, so that -- the issue is the particles that are
14 formed from vapors may have significant toxicity that is
15 not generally understood when you have a traditional kind
16 of soot particles that you're referring to.

17 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
18 I think that would be very helpful, Dr. Froines, to get
19 those papers.

20 --o0o--

21 MR. KRIEGER: In summary, ETS is a complex
22 mixture of gases and particles, many with known adverse
23 health effects. Tobacco smoke contributes several tons
24 per year of nicotine, fine particles and carbon monoxide
25 into the California atmosphere. Most ETS particles range

1 in size from .01 to 1 microgram.

2 Although most of the non-smoking public's
3 exposure to ETS is low, in certain cases outdoor exposures
4 can be significant, ranging up to 4.6 micrograms per cubic
5 meter in nicotine. Indoor ETS nicotine concentrations may
6 range from .5 to 76 micrograms per cubic meter.

7 Use of biomarkers are a good predictor of ETS
8 exposures.

9 And daily exposures to ETS nicotine
10 concentrations can range from less than 1 to 3 micrograms
11 per cubic meter.

12 PANEL MEMBER BLANC: What do you mean when you
13 say significant?

14 MR. KRIEGER: Oh, significant, when we referred
15 to the outdoor concentration of 4.6?

16 PANEL MEMBER BLANC: Yeah, what does significant
17 mean in that sense?

18 MR. KRIEGER: Significant means that -- from our
19 standpoint, significant is an exposure level that's equal
20 to some concentrations that are found indoors. The 4.6 is
21 significant compared to an outdoor of low exposure.

22 PANEL MEMBER BLANC: So when you say the
23 sentence, what you really mean is indoor -- I'm sorry. So
24 the point -- is that supposed to be indoor ETS nicotine --

25 MR. KRIEGER: Yeah, indoor.

1 PANEL MEMBER BLANC: Okay. So that's supposed to
2 say indoor, right?

3 CHAIRPERSON FROINES: Which one are you on?

4 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
5 Yeah, the third bullet from the bottom?

6 PANEL MEMBER BLANC: So then why are you going
7 from outdoor to indoor? Why wouldn't you go from indoor
8 to outdoor, for example? Is the argument -- what's the
9 logical argument here?

10 MR. KRIEGER: I'm looking at the -- oh, we're
11 talking about the fourth bullet down, right?

12 PANEL MEMBER BLANC: The third bullet from the
13 bottom, "Indoor ETS nicotine concentrations present
14 significant exposures ranging from .5 to 76."

15 MR. KRIEGER: Oh, the "significant" would be
16 actually the upper end of that range. It would be the 76.

17 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
18 Yeah.

19 PANEL MEMBER BLANC: So then you're saying that
20 the bullet before that, the significance of the outdoor is
21 not significant because it doesn't get up to 76?

22 MR. KRIEGER: No, I think we -- we need to
23 clarify that point. Actually the 4.6, the outdoor
24 concentration, is significant, is compared to those
25 concentrations generally found indoors. The slide before,

1 the table, indoor concentrations on average had .5 to 6
2 micrograms per cubic meter.

3 The 76 micrograms per cubic meter for the indoor
4 concentration was -- basically the betting established
5 those of the priors. So that's the very high end of the
6 range.

7 But the 4.6 outdoor concentration is significant
8 that it falls right in between the middle of the indoor
9 exposure --

10 PANEL MEMBER BLANC: So it's not that the word is
11 not "significant". In the bullet before then what you
12 mean is that outdoor exposures can be substantive and fall
13 within a range that is commonly found indoors. Is that
14 what you mean?

15 MR. KRIEGER: That's correct, that's correct.

16 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
17 That's the point we're trying to make.

18 CHAIRPERSON FROINES: I think we have a tendency
19 to overuse the word "significant". And probably leaving
20 the word "significant" out would -- and let the data stand
21 on its own, or if there's some explanation to explain it.
22 But I think the word "significant" tends to mean different
23 things with different people.

24 PANEL MEMBER BLANC: And I think you need to
25 reverse the order here, because if you're building up the

1 argument that the reason it's substantive is because it
2 approaches the indoor levels, then you should tell us what
3 the indoor levels are first. It's not a logical sequence
4 here.

5 MR. KRIEGER: Okay.

6 PANEL MEMBER BLANC: I mean I understand this is
7 a slide for us. But assuming that this somehow may appear
8 in some other summary recitation.

9 MR. KRIEGER: Okay. Good point.

10 Next slide.

11 --o0o--

12 MR. KRIEGER: Before we go on to OEHHA's
13 presentation, we have summarized a few of the major -- or
14 the major comments that we received on the Part A exposure
15 assessment. In general they fall into four categories.

16 First, we have several comment letters in support
17 of our report and the identification of ETS as a TAC.

18 Next, in the exposure assessment portion of the
19 report, a comment centered around the contention that the
20 draft report does not address the specific exposures that
21 cause adverse health effects. Our response is that we
22 believe there is sufficient evidence presented in the
23 report to show that ETS is admitted into the ambient air
24 in California and that there are adverse health-related
25 impacts to exposures to ETS.

1 Another comment suggested that short-term
2 exposures are inadequate to assess long-term
3 population-weighted exposures. As we talked about before,
4 we used a scenario-based approach to estimate daily
5 concentration for a range of subpopulations. Since ETS
6 sources are localized, we felt it better to estimate a
7 measure of daily exposure. A population-weighted
8 assessment would not adequately address the public's
9 exposure, especially those subgroups that are being
10 exposed to higher ETS concentration levels.

11 --o0o--

12 MR. KRIEGER: The next category of comments
13 address ARB's monitoring study. A commenter mentioned
14 that ARB's monitoring study did not measure exposure
15 duration and its use of nicotine as a marker has problems.
16 Again, the purpose of our monitoring study was to estimate
17 exposures near smoking sources. We took one-hour and
18 eight-hour samples to estimate more realistic daily
19 exposure scenarios.

20 The use of nicotine in the outdoor environment
21 has been done before, and we believe this method used to
22 collect the samples was accurate and reliable.

23 --o0o--

24 MR. KRIEGER: Next comment. The staff should
25 consider the personal monitoring results from the 16-city

1 study done by Jenkins.

2 We added the personal exposure results to this
3 study into our indoor section of the report.

4 The next comment. The commenter suggests that
5 cotinine is not a particularly quantitative indicator of a
6 person's nicotine exposure.

7 At this time the scientific community accepts the
8 basis that cotinine and nicotine are reasonable indicators
9 of a person's relative degree of exposure to tobacco
10 smoke. Several studies referenced in Part A exposure
11 assessment used cotinine as a sufficient indicator of ETS
12 exposures.

13 --o0o--

14 MR. KRIEGER: The last major comment focused on
15 our authority to identify ETS as a whole since its makeup
16 changes over time. We believe that it is reasonable to
17 consider ETS holistically as a toxic air contaminant as it
18 is emitted from a common source. The ARB used this
19 approach in the past when evaluating diesel exhaust as a
20 toxic air contaminant. They included information on the
21 atmospheric persistence of the ETS compounds because it is
22 important to point out that a chemical nature of ETS has a
23 temporal effect.

24 --o0o--

25 MR. KRIEGER: Now, before I turn it over to

1 Melanie for OEHHA's presentation I would like to go over
2 the next steps in the identification process, as shown in
3 this slide.

4 If the Panel is still deliberating about the ETS
5 report after today's meeting, a second meeting will be
6 needed.

7 If you approve the report at the next meeting,
8 you would prepare and send findings on the report to the
9 ARB.

10 Once we receive the SRP findings, the ARB
11 initiates the rulemaking process with the public release
12 of the hearing notice and the staff report, which contains
13 the staff proposal to list ETS as a TAC. The public is
14 then given a 45-day comment period on the initial
15 statement of reasons.

16 And the process culminates with the Board hearing
17 to considering identifying by regulation ETS as a TAC.

18 And that concludes my presentation.

19 Any questions on that before we go to Melanie?

20 CHAIRPERSON FROINES: I think it would have been
21 useful to have seen in your presentation some of the data
22 that you actually collected. It seemed a little thin in
23 terms of the presentation to me.

24 PANEL MEMBER BLANC: Well, they did present some
25 of the data at a previous meetings, isn't that correct?

1 The actual sampling data from Sacramento. You might want
2 to just have just perhaps more -- at our January meeting
3 you may want to just remind us of some of the key original
4 studies that you did. So I think that's what you --

5 CHAIRPERSON FROINES: Jim, can you make a note of
6 that, to follow up on that?

7 MR. KRIEGER: We can do that.

8 PANEL MEMBER BLANC: And is there a -- forgive me
9 for asking certain questions, which betray a lack of total
10 familiarity with the draft document. But remind me, is
11 there a table in your exposure document which lists the
12 known constituents which are already designated as TACs?
13 That's in there, isn't it? We talked about that before.

14 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
15 That's in there.

16 PANEL MEMBER BLANC: So that addresses the one --
17 also doesn't that address one of those -- the critical
18 comments that you received?

19 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
20 Yes.

21 CHAIRPERSON FROINES: Is there a table -- and I'm
22 sorry. I apologize for the same reason. Is there a table
23 that looks at the size distribution of the particulate?

24 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
25 There is, as a matter of fact.

1 CHAIRPERSON FROINES: And I just don't remember.
2 And I didn't want to take time to look. I'll have to
3 worry about it.

4 ARB SUBSTANCE EVALUATION SECTION MANAGER AGUILA:
5 Yeah, there's actually a table that summarizes some of the
6 key studies that we looked at. And then there was also a
7 graph from a Morasco study, kind of indicates --

8 CHAIRPERSON FROINES: That's fine.

9 Peter, where are we in terms of lunch?

10 MR. MATTHEWS: It's soon coming.

11 CHAIRPERSON FROINES: Is that -- could you check
12 and see if the person peaking through the door is lunch.

13 MR. MATTHEWS: They're coming in.

14 CHAIRPERSON FROINES: Because if the lunch is
15 here, we could take a short break and then we can get
16 started with Melanie and OEHHA.

17 MR. MATTHEWS: They're coming in.

18 CHAIRPERSON FROINES: They are?

19 Well, let's take a break, get some sandwiches,
20 and come back and Melanie will get started.

21 I think -- unless there are more questions for
22 ARB right now.

23 No?

24 (Thereupon a recess was taken.)

25 CHAIRPERSON FROINES: Is everybody on the Panel

1 here?

2 Before we continue I want to make one statement
3 basically for the record. And, that is, that the Panel
4 has received a letter dated November 16th, 2004, from an
5 attorney representing R.J. Reynolds Tobacco Company. In
6 the letter the company claims that panel members qualified
7 as pathologists or oncologists must also be medical
8 doctors; and that Drs. Glantz and Hammond have engaged in
9 certain professional activities which cast doubt on their
10 ability to review the draft report objectively.

11 So I have consulted with SRP's legal counsel on
12 this issue. And I have been advised that nothing in the
13 R.J. Reynolds letter prevents the panel from moving
14 forward on the draft report.

15 The Health and Safety Code does not require a
16 medical degree for one to be qualified as an expert in
17 pathology or oncology.

18 Further, the lawyer has concluded that Drs.
19 Glantz and Hammond do not have conflicts of interest in
20 the matter at hand.

21 I've spoken with Stan and -- Dr. Glantz and
22 Hammond, and they both assured me that they will be able
23 to fairly and objectively participate in the Panel's
24 review of the draft report.

25 I'm satisfied with those assurances and believe

1 the Panel should move forward on the consideration of the
2 report.

3 So we are going to reject the contentions of the
4 R.J. Reynolds letter and we can move forward.

5 (Thereupon an overhead presentation was
6 Presented as follows.)

7 OEHHA DEPUTY DIRECTOR ALEXEEFF: Hi. This is
8 George Alexeeff, Deputy Director of OEHHA. I just wanted
9 to make a couple of comments.

10 One is we did a very extensive, thorough,
11 comprehensive evaluation of environmental tobacco smoke
12 over the last two to three years. It utilized probably up
13 to about ten or more staff members in various ways. And
14 we feel -- although it's been referred to or might be
15 called an update, we feel it's a very thorough,
16 comprehensive report. We're very proud of this report and
17 think it has identified a number of very important
18 scientific issues and public health issues. And so we're
19 just -- we know you'll have a number of issues that you'll
20 raise. But we feel very proud and very happy to bring
21 this report to you today.

22 SUPERVISING TOXICOLOGIST MARTY: With that I'm
23 going to start by going through the introduction to the
24 document. And we do have a presentation on each chapter.
25 Since time is sort of critical today, I will reserve the

1 right to skip some of the slides in the hopes of just
2 giving a reasonable overview of the material that's in the
3 document.

4 --o0o--

5 SUPERVISING TOXICOLOGIST MARTY: The Children's
6 Health Act of 1999 in California did amend the toxic air
7 contaminant statutes mandating OEHHA to explicitly
8 consider exposure patterns and special susceptibility of
9 infants and children when developing health effects
10 assessments of toxic air contaminants.

11 It's worth noting that ETS has a number of
12 adverse health effects on infants and children, including
13 sudden infant death syndrome, asthma induction and
14 exacerbation, increased lower respiratory tract
15 infections, and impacts on decrements in berth weight.

16 Therefore if the panel chooses to recommend that
17 ETS be added as a TAC, we think it should be added to the
18 list of TAC that disproportionately impact infants and
19 children pursuant to Health and Safety Code Section
20 396669.5.

21 --o0o--

22 SUPERVISING TOXICOLOGIST MARTY: The approach
23 OEHHA used to updating our '97 health effects assessment
24 focused essentially on epidemi --

25 CHAIRPERSON FROINES: Melanie, I'm sorry. I

1 don't mean to interrupt, and I'll try and be quiet.

2 But just as a matter of policy -- and this may be
3 for George -- every time we now see a document from you,
4 can we make that determination were the evidence to
5 warrant it? In other words, we went through the five
6 chemicals, and we listed another group of chemicals that
7 didn't meet the requirements, didn't meet the -- have
8 sufficient evidentiary basis. And so the point is: Is it
9 as a matter of law and policy that we can with each
10 chemical make that determination?

11 SUPERVISING TOXICOLOGIST MARTY: The law actually
12 requires OEHHA to update the list. So if OEHHA makes the
13 recommendation, then the list gets updated. I think the
14 panel can weigh in as to whether that TAC should be on the
15 list of those that disproportionately impact infants and
16 children.

17 CHAIRPERSON FROINES: So this could be a method
18 to update the list?

19 SUPERVISING TOXICOLOGIST MARTY: Correct.

20 OEHHA DEPUTY DIRECTOR ALEXEEFF: And --

21 CHAIRPERSON FROINES: Beyond five?

22 OEHHA DEPUTY DIRECTOR ALEXEEFF: Yeah. This
23 is George Alexeeff again.

24 Of course this compound is being brought to you
25 through the TAC process. So every compound brought

1 through the TAC process should be evaluated for its impact
2 on children. Any recommendations you have regarding
3 either endpoints or health issues that address that issue
4 would be very helpful for us in terms of adding in the
5 process. Since we haven't actually added one to the list
6 by this process yet, we'll probably just be working it out
7 with the Air Board once we add one. And then we'll know
8 all the different particulars.

9 But any -- as Melanie mentioned, we do have to
10 update the list. And this would be, you know, a candidate
11 for updating the list. Or it could be the next compound
12 that updates the list, depending upon how the panel
13 concludes its review and how the -- you know, the
14 chemicals listed as a TAC.

15 SUPERVISING TOXICOLOGIST MARTY: To be noted, the
16 list updates have to go through panel review. So we do
17 have a significant role.

18 In our approach to updating the '97 health
19 effects assessment we focused primarily on the
20 epidemiology studies rather than the animal toxicology.
21 So the chapters describe new epidemiology studies
22 published since the previous document was written. And we
23 did use animal toxicology information to support specific
24 health outcomes.

25 --o0o--

1 SUPERVISING TOXICOLOGIST MARTY: We conducted
2 literature searches basically from '96 forward using a
3 variety of search terms, including passive smoking, ETS,
4 side-stream smoke and so on.

5 We described the more important epidemiological
6 studies in each of the chapters.

7 Chapters 3 through 5 deal with developmental and
8 reproductive health effects. Chapter 6 deals with the
9 respiratory tract. Chapter 7 is carcinogenicity. And
10 Chapter 8 is cardiovascular health effects.

11 --o0o--

12 SUPERVISING TOXICOLOGIST MARTY: When we
13 evaluated studies we focused on study quality, looking at
14 thing such as: Sample size; the ability to ascertain
15 exposure and associated problems with misclassification of
16 exposure; and then potential confounding and how the
17 studies dealt with that; and as well as sources of bias.

18 --o0o--

19 SUPERVISING TOXICOLOGIST MARTY: As in the last
20 evaluation, we used what we term a "weight-of-evidence"
21 approach.

22 An effect is judged to be causal when positive
23 associations between ETS exposure and effect is observed
24 in studies in which chance, bias, and confounding can be
25 ruled out with reasonable confidence.

1 We examined the body of the studies for:

2 Consistency from study to study.

3 For biological plausibility; and this is where
4 the animal studies did play an important role.

5 And for bias and confounding as ways to explain
6 the results.

7 --o0o--

8 SUPERVISING TOXICOLOGIST MARTY: We did find that
9 the evidence was sufficient to say there is a causal
10 association between ETS and developmental effects
11 including SIDS and fetal growth. We thought the data were
12 sufficient for a number respiratory endpoints including
13 acute lower respiratory infections in children, asthma
14 induction and exacerbation in children and adults, chronic
15 respiratory symptoms such as bronchitis in children and
16 otitis media. And, finally, we looked at the carcinogenic
17 effects. And we continue to believe the data are
18 sufficient for a causal association between ETS and lung
19 cancer and also nasal sinus and now breast cancer. Breast
20 cancer is a new finding.

21 PANEL MEMBER BLANC: Melanie, can you go back to
22 the previous slide for a second.

23 When you're -- you're not using the terms here.
24 But you're clearly trying to be consistent with sort of
25 classic Bradford-Hill criteria.

1 And one of the issues that comes up in various
2 chapters or with various issues, although not
3 consistently, is the issue of whether or not an effect
4 which is consistent with direct cigarette smoking is
5 evidence of a dose response. I mean it's a sort of
6 implicit issue that comes up.

7 And in certain -- in responses to certain
8 critiques you get into arguments about -- or discussions
9 as to ways in which it might not be -- certainly not a
10 linear dose response, and perhaps even not ordinal dose
11 response.

12 Is that safe to say?

13 SUPERVISING TOXICOLOGIST MARTY: Yes, that's safe
14 to say.

15 PANEL MEMBER BLANC: And yet it seems to -- the
16 issue seems to come up in these context-specific ways, but
17 not in a very general way at the same point in which
18 you're discussing sort of the Bradford-Hill criteria.
19 Would it not strike them -- the document even if it was
20 somewhat competitive to have an overall discussion of the
21 dose response -- of what dose response -- of the
22 implications of the relationship between findings with
23 active smoking versus findings with secondhand smoke in
24 terms of dose response as an argument for causality.

25 SUPERVISING TOXICOLOGIST MARTY: Yeah, I think we

1 did try to do that. Wherever we had dose response
2 formation we pointed that out.

3 PANEL MEMBER BLANC: But that's dose response
4 within higher or lower ETS, isn't it? It's not dose
5 response -- because for all of these things there are
6 studies which talk about direct smoking.

7 SUPERVISING TOXICOLOGIST MARTY: Right. We did
8 talk about direct smoking for most of the health
9 endpoints, and whether or not there was an effect with
10 direct smoking.

11 The one health endpoint where we don't think that
12 dose response is particularly linear is with breast
13 cancer. And we'll get into that in a few slides. So we
14 did talk about dose response not being linear because of
15 these other issues associated with active smoking. And
16 those affect -- the effect of the act of smoking on breast
17 cancer risk is various susceptible sub-populations related
18 to antigenicity --

19 PANEL MEMBER BLANC: And I'm not saying you
20 shouldn't have that discussion there. I guess what I'm
21 saying is: Is there a global discussion that you should
22 have?

23 SUPERVISING TOXICOLOGIST MARTY: You know, it
24 almost didn't come up except for there, because --

25 PANEL MEMBER GLANTZ: Yeah, I think that the --

1 it also is an issue when you talk about cardiovascular
2 effects and the trying to do a -- and that brings up the
3 whole issue of what are people talking about in terms of
4 so-called cigarette equivalence.

5 And I really think that's not a productive way to
6 look at this, because there's so many different ways, so
7 many different compounds in cigarette smoke, that what you
8 get as your, quote, cigarette equivalent is highly
9 dependent on what compound you're measuring.

10 So I think that the idea of dose response and
11 trying to make the active smoking and the passive smoking
12 stuff -- to kind of put them on the same scale would be
13 very misleading because the secondhand smoke is a complex
14 compound and it's different from the mainstream smoke.

15 PANEL MEMBER BLANC: But doesn't that argument --
16 if that's going to be the argument, doesn't that argument
17 need -- isn't that I primal enough argument that needs to
18 be made early in the document?

19 PANEL MEMBER GLANTZ: Well, you know, I guess. I
20 mean I can't -- I've been through the document a few times
21 and I know these arguments are in there somewhere.

22 SUPERVISING TOXICOLOGIST MARTY: Yeah, we could
23 pull them forward.

24 PANEL MEMBER BYUS: Well, I also agree with Paul.
25 And that was one of the -- you constantly go back and

1 forth between primary smoking and ETS. And you -- which
2 is a good thing to do. Don't get me wrong. I think it's
3 a good thing. But you really need to try and discuss what
4 the limitations on that kind of association are, if there
5 are any.

6 And then also dose response, I would disagree
7 with you. I mean I think trying to -- establishing a dose
8 response is the gold standard of establishing causality.
9 And so you're referring to a constant -- you're repeatedly
10 referring to dose response relationships between ETS and
11 primary smoking is a good thing to do, except if there are
12 limitations in the overall strategy. I think if you lay
13 that out initially, as Paul suggests, that it would allow
14 your arguments to be easier to follow as you go through
15 the document.

16 SUPERVISING TOXICOLOGIST MARTY: All right.
17 We'll put that into the introduction section and a little
18 discussion bringing that forward. That's a good point.

19 PANEL MEMBER GLANTZ: Just the point I was trying
20 to make -- I mean I think if you do find a dose response,
21 that strengthens your argument. The issue I was trying to
22 raise was trying to go between dose of active smoking and
23 dose of passive smoking, that and the idea of having
24 cigarette equivalent type things. And I think that's very
25 problematic. I think within looking at active smokers or

1 passive smokers, if you see a dose response effect, that's
2 a very -- that strengthens your argument. It's just
3 trying to extrapolate from active smoking down to passive
4 smoking, which is where I think you get into trouble, at
5 least with some endpoints like heart disease.

6 PANEL MEMBER BLANC: So I think it would be --
7 just to clarify what it was that I implied in this
8 discussion would be, if you couldn't lay out for the
9 reader in general we -- you know, obviously dose response
10 is a key part of our causal assessment, that we have
11 certain general principles in terms of looking at active
12 smoking as a dose -- in a dose response way that in --
13 pour out comes for which we have no reason to believe that
14 it would not be an ordinal relationship, we will -- you
15 will see that we will use it as an argument for dose
16 response in situations where we believe it's ordinal.

17 But we have strong reasons to believe it's not
18 linear where there may be a steep step up early on such as
19 cardiovascular. We make that clear. In areas where we
20 think in fact it's not even ordinal, because of anti --
21 you know, estrogenal -- anti-estrogenal effects that high
22 exposure such as with active smoking, which may be
23 relevant to endocrine-related malignancy and promotion, we
24 will make that clear as we go forward. Because,
25 otherwise, it's just odd not to be -- to be avoiding the

1 issue as head-on at the beginning.

2 SUPERVISING TOXICOLOGIST MARTY: Okay. So we
3 also noted that we think the evidence is sufficient for a
4 causal association between ETS exposure and the number of
5 cardiovascular effects, including heart disease
6 mortality -- heart disease morbidity and altered vascular
7 properties.

8 And also there are a number of other health
9 endpoints that we think there is evidence that there is
10 suggestive associations between ETS exposure amongst other
11 endpoints.

12 --o0o--

13 SUPERVISING TOXICOLOGIST MARTY: We updated some
14 of my attributable risk calculations where data permitted.
15 And these are all presented in Table 1.2 for a number
16 of endpoints.

17 --o0o--

18 SUPERVISING TOXICOLOGIST MARTY: And this is
19 Table 1.2. And what we have presented is the excess
20 number of cases attributable to ETS exposure for those
21 health endpoints in California and then an estimate for
22 the excess in the United States. And there's a lot of
23 description in the document about how those numbers were
24 calculated.

25 --o0o--

1 SUPERVISING TOXICOLOGIST MARTY: I'd like to go
2 through each chapter. What I want to do though is -- I
3 may not do it in order. So I'm going to start with
4 Chapter 3, which is perinatal manifestations of
5 developmental toxicity. And depending on how time is
6 moving on, we really should get through Chapters 6 and 7
7 today since they have the two endpoints that have jumped
8 to conclusive.

9 CHAIRPERSON FROINES: Do those estimates that
10 you've just showed on the slides, do they -- do they then
11 meet the requirement for some estimate of risk, in your
12 view?

13 SUPERVISING TOXICOLOGIST MARTY: That is how we
14 approached --

15 CHAIRPERSON FROINES: The question was raised by
16 one of the commenters.

17 SUPERVISING TOXICOLOGIST MARTY: Right. That is
18 how we approached risk in the context of the ETS, rather
19 than generating a universal factor or even attempting to
20 do that.

21 CHAIRPERSON FROINES: Good.

22 SUPERVISING TOXICOLOGIST MARTY: The first slide
23 of each of these chapter discussions is essentially the
24 table in the beginning of the chapter. That looks at the
25 health outcome; the number of studies that we reviewed for

1 the '97 document; the number of additional studies in the
2 update; and whether we think there is sufficient evidence
3 of causal association, is it suggestive, is it
4 inconclusive or is it conclusive?

5 In this particular table we're describing ETS and
6 pregnancy outcomes. And essentially we think the newest
7 studies strengthen the conclusions of the '97 report
8 regarding effect on low birth weight and birth weight
9 decrement, pre-term delivery, and intrauterine growth
10 retardation.

11 CHAIRPERSON FROINES: Can I just say that I
12 thought this approach that you had consistently with each
13 chapter starting off with that tabular presentation was
14 extremely helpful.

15 SUPERVISING TOXICOLOGIST MARTY: Thanks.

16 This slide is designed to give you a bird's-eye
17 view of the information reported in the literature on mean
18 change in birth weight. The change is on the Y axis, and
19 it's in grams. The X axis is essentially each of the
20 studies that looked at that.

21 You can note that there are a number of studies
22 which indicate a depression in mean birth weight in the
23 ETS exposed groups in these studies relative to
24 non-exposed. And that many of these are statistically
25 significant; for example, the diamonds that are filled in

1 are statistically significant estimates.

2 In some of the studies, they broke out the groups
3 by age. For example, Ahluwalia, which is in our update.

4 It's that point -- where am I?

5 The 30 -- the greater than 30-year-old women
6 actually had babies that were -- had birth weight
7 decrements. But the younger-than-30-year-old women did
8 not. So it kind of is an indication of susceptible
9 sub-populations.

10 And there are a number of very well conducted
11 studies that had all those small decrements in birth
12 weight such as Marty Kharrazi's study here and Dejmek's
13 study here. There were small but significant birth weight
14 decrements.

15 And I think I should make a comment that these
16 small birth weight decrements may be in and of themselves
17 to an individual not especially important, unless they're
18 already small babies and you're pushing them into the
19 low-birth-weight high risk category and all of the
20 associated health outcomes of low -- from having low birth
21 weight.

22 --o0o--

23 SUPERVISING TOXICOLOGIST MARTY: In addition,
24 there were a couple of meta-analyses published.

25 Gayle Windham published one, in which she looked

1 at studies for North America. And these studies that she
2 chose and the eight that she ended up choosing assessed
3 multiple sources of exposure to the mother rather than
4 just, "Does your spouse smoke?" And they also had
5 adjusted for a number of important confounders. And she
6 finds the birth weight decrement of 24 grams. That's
7 statistically significant.

8 Peacock, et al., also published a meta-analysis
9 along with her own original study. And she pulled
10 estimates from 11 studies that had also adjusted for
11 confounders and gets a birth weight decrement in a similar
12 range. Also statistically significant.

13 And in both of these meta-analysis there was no
14 evidence of paragenetics. So they thought they were
15 dealing with a homogenous group of studies.

16 --o0o--

17 SUPERVISING TOXICOLOGIST MARTY: This slide just
18 shows an overview of the data on ETS and risk of low birth
19 weight. So in this case we're looking at an odds ratio of
20 having a baby that's less than 2500 grams, which is the
21 standard definition of low birth weight. And, again, it's
22 interesting to see that there appears to be some
23 differences by maternal characteristics.

24 Ahluwalia again looked at women 30 years old and
25 greater. And they had a very statistically significant

1 odds ratio of low birth weight compared to younger women
2 in that study.

3 And Gayle Windham looked at whether you were --
4 what race you were. And if you were non-Caucasian, there
5 was also a very significant risk odds ratio for low birth
6 weight.

7 --o0o--

8 SUPERVISING TOXICOLOGIST MARTY: So you can see
9 that there are a number of studies that have elevated
10 risks. Some are statistically significant. There was one
11 meta-analysis published again by Windham. And she
12 combined low birth weight and small for gestational age.
13 She looked at 11 studies and got pooled risk estimates
14 that were statistically significant and elevated. And
15 then for three of the studies that she had determined had
16 the best exposure and confounder adjustment. Their at the
17 pool estimate was higher.

18 --o0o--

19 PANEL MEMBER BLANC: Well, then this is another
20 generic question that will come up throughout.

21 When you have a luxury of a meta-analysis that's
22 been published in the interim, where do you count it when
23 you talk about a number of additional studies in update?
24 Is it in the total number of studies? Is it --

25 SUPERVISING TOXICOLOGIST MARTY: No, it's not.

1 It's not. Those -- the number of studies in the update I
2 believe are just the original -- new original studies. In
3 both those cases, Windham and Peacock, they did original
4 study, and they also included a meta-analysis in their
5 paper.

6 PANEL MEMBER PLOPPER: So you count it as an
7 original study?

8 SUPERVISING TOXICOLOGIST MARTY: Yeah, so
9 their -- we counted their original study.

10 PANEL MEMBER BLANC: As original studies.
11 That was in the same publication. They did a
12 meta-analysis at the same --

13 SUPERVISING TOXICOLOGIST MARTY: Correct, right.

14 And I should note also that these slides, looking
15 at an overview picture, these are the overall odds ratios.
16 And some of those papers had separated out groups by other
17 methods and had different odds ratios according to
18 maternal factors.

19 In the case of Ahluwalia, she didn't do an
20 overall. She did a greater than 30, less than 30. So
21 that's why they're both up there on that slide.

22 PANEL MEMBER BLANC: But they're not counted as
23 two studies?

24 SUPERVISING TOXICOLOGIST MARTY: No, it's not
25 counted as two studies.

1 PANEL MEMBER BLANC: So in fact if you wanted to
2 put a little asterisk and, say, below the table, this does
3 not even include two meta-analyses, that will be put in
4 later, I mean it does strengthen your -- there are two
5 positive meta-analyses, right?

6 PANEL MEMBER HAMMOND: Or you can put another
7 line down set met analyses data and put it on the graph.

8 SUPERVISING TOXICOLOGIST MARTY: Can put it on
9 the graph, yes --

10 PANEL MEMBER HAMMOND: But it's a separate thing
11 from the individual.

12 SUPERVISING TOXICOLOGIST MARTY: Okay. Put them
13 on the graph.

14 Okay. This is an overview of some of the studies
15 that looked at small for gestational age, which is
16 generally identifies less than a 10th percentile of body
17 weight for that gestational age. And most people use it
18 synonymously with IUGR, intrauterine growth retardation.

19 And you can see that there are some suggestive
20 studies that there is an effect, some of the risk
21 estimates are elevated. A couple of them are even
22 statistically significant. There is one more study which
23 we didn't put on here because it was from India. They had
24 a very significant elevation, an odds ratio of 2.1. But
25 it was indian tobacco and they put other stuff in there

1 besides tobacco. It's not what you're thinking. Charcoal
2 and some other kind of funny things.

3 And then also their cigarettes aren't really like
4 American cigarettes. They're wrapped in other plant
5 leaves, which aren't tobacco and -- who knows what they
6 are. So we didn't include it on this table. But if we
7 did, that would be yet another statistically
8 significant --

9 PANEL MEMBER BLANC: When you referred to it in
10 the text, then why is it you don't include it --

11 SUPERVISING TOXICOLOGIST MARTY: We had to put
12 that in. We didn't say why didn't want to put it in the
13 text. I realized that yesterday. But we should.

14 PANEL MEMBER BLANC: You mean it's not in the
15 text either?

16 SUPERVISING TOXICOLOGIST MARTY: The study is
17 described in the text. But we didn't explain why we
18 didn't put it on the table.

19 PANEL MEMBER BLANC: So you should add the point
20 in which you refer to it in the text.

21 SUPERVISING TOXICOLOGIST MARTY: We should do
22 that.

23 --o0o--

24 SUPERVISING TOXICOLOGIST MARTY: Okay. So
25 we're --

1 PANEL MEMBER BLANC: There's no -- and then you
2 haven't come across a formal meta-analysis of these data?

3 SUPERVISING TOXICOLOGIST MARTY: There may have
4 been one that combined -- yes, there one that combined SGA
5 with low birth weight. That was the Windham paper. And
6 she felt she could do that because the low birth weight
7 study she used had adjusted for gestational age, which is
8 an important confounder for low birth weight. So she
9 combined both of those into one, which was actually the
10 previous slide we showed.

11 --o0o--

12 SUPERVISING TOXICOLOGIST MARTY: That one.
13 Exactly.

14 --o0o--

15 SUPERVISING TOXICOLOGIST MARTY: Okay. So we
16 considered that, and was suggestive of an association
17 between ETS and small for gestational age or intrauterine
18 growth retardation. And this actually is an interesting
19 study on why tobacco smoke would do that.

20 Next slide please.

21 --o0o--

22 SUPERVISING TOXICOLOGIST MARTY: ETS and risk of
23 preterm delivery. Again here we have a number of studies
24 which showed elevated risk. And the filled-in ones were
25 statistically significant elevated risk. And, again, over

1 30 years old you seem to have a larger issue with
2 association with ETA. And whether that's because you've
3 been exposed for a longer period of time than the younger
4 women, no one's really sure.

5 And, again, for Windham's study she's found that
6 non-white women had a higher risk of preterm delivery with
7 ETS exposure than white women.

8 And Marty Kharrazi finds an overall elevated risk
9 of preterm delivery.

10 There's actually an additional study in which the
11 Panel can think about. It's Yuan et al and -- 2001. They
12 divvied up their women by hair and nicotine levels. And
13 we had some issues with how they did their hair and
14 nicotine analysis, which we can talk to the panel about at
15 some point. But they also had an elevated odds ratio of
16 6, which was statistically significant. So that would be
17 a fourth data point on there that was statistically
18 significant. At this point we're calling this suggestive
19 evidence rather than --

20 PANEL MEMBER BLANC: Can we -- I'd like to hear
21 for a second from the leads on this document at this
22 particular point. What is it that you would need for this
23 to be more than suggestive? And how did the two leads
24 read this particular section?

25 PANEL MEMBER BYUS: The preterm delivery or the

1 entire --

2 PANEL MEMBER BLANC: No, the preterm delivery,
3 because it's --

4 PANEL MEMBER PLOPPER: Why they -- why do they
5 make the choice between suggestive and --

6 PANEL MEMBER BYUS: Yeah. It's difficult. I
7 have no problems with the low birth weight. I thought
8 that data was extremely persuasive, the fact that you can
9 have -- even if it's small, it's extremely to me
10 significant of something happening if you can affect the
11 birth weight. I mean you can do a lot of things -- at
12 least in animal studies -- we've done a lot of animal
13 studies where you can do a lot to animals but not affect
14 birth weight at all. So the fact that the birth weight is
15 being affected is very, very persuasive to me about the
16 risk of environmental tobacco smoke.

17 In terms of this data, it's a little harder for
18 me to follow it and the significance of it. And I was
19 impressed by that nicotine and the hair, when you bend the
20 data out that way and got that extreme risk factor. So I
21 would be interested in hearing your explanation of that.

22 SUPERVISING TOXICOLOGIST MARTY: Yeah, we're
23 taking another look at that study and trying to decide
24 whether we need to put that up there as well.

25 CHAIRPERSON FROINES: But Paul's raising a

1 specific but also generic issue, which is quite simply how
2 do you decide when something is sufficient. I think
3 that's an accurate statement.

4 PANEL MEMBER BLANC: Yeah, because -- I look at
5 the left side of this and I say, okay, I see why in 1997
6 they had five studies. None of them were statistically
7 significant. The point estimate was less than 1 in one
8 study. The point estimate was essentially 1 in another
9 study. An the point estimate was elevated in three
10 studies, none of them -- so, okay, suggestive because --
11 and suggestive is, you know, pretty mild. Now I see 1, 2,
12 3, 4 -- I see 1, 2, 3, 4 studies, two of which have
13 stratified analyses. Each study is positive in at least
14 one strata in the direction. Two of the studies have
15 substrata that stratify parts of them that are
16 statistically significant. One has a -- the whole study
17 is statistically significant. Kharrazi is statistically
18 significant. One of them is quite close to -- I don't
19 know -- Horta, is that statistically significant also?

20 SUPERVISING TOXICOLOGIST MARTY: No, it was not.

21 PANEL MEMBER BLANC: But it's very close.

22 SUPERVISING TOXICOLOGIST MARTY: Close.

23 PANEL MEMBER BLANC: And now you're telling me
24 there's a study you don't have on here because you weren't
25 fully satisfied with the -- but it's from Jaakkola, right.

1 SUPERVISING TOXICOLOGIST MARTY: Yes, it's
2 Jaakkola.

3 PANEL MEMBER BLANC: And so it's like the premier
4 ETS research group in the world has this study, which is
5 positive. And I looked at this and I said well -- you
6 know, boy, that if -- you know, you could say very, very,
7 very, very suggestive. But what else is it that you want?
8 I mean is this a situation in which you guys are trying to
9 do some kind of internal meta-analysis is what is required
10 for you to go from -- to cross the Rubicon in to
11 conclusive?

12 SUPERVISING TOXICOLOGIST MARTY: We'll wade into
13 the Rubicon and see what we can do.

14 PANEL MEMBER BLANC: Get your feet wet?

15 CHAIRPERSON FROINES: You know, the thing is --
16 it's always been interesting to me that different
17 regulatory groups or risk assessment groups talk about
18 using the weight-of-evidence approach. But I never have
19 understood what the weight is. Be a quantitative way to
20 approach, if you did a -- which is what we normally do
21 with meta-analysis. And so it seems to me that in this
22 case it may be that you have to do at least some rough
23 estimate of meta-analysis or develop criteria where some
24 weight is sufficient. Otherwise the weight is rhetorical,
25 I think.

1 PANEL MEMBER GLANTZ: Well, I think here you
2 should just do the meta-analysis. It's not that hard if
3 you've got all the data you need. And there are --

4 PANEL MEMBER BLANC: How do you do it when you
5 have -- when an author has only provided you with two
6 stratified things? You treat them as completely separate
7 studies of meta-analysis?

8 PANEL MEMBER GLANTZ: Well, you can do it
9 different ways. I mean some people will try to recombine
10 them and other people will treat them as separate studies.
11 They're separate groups of people. And the sample sizes
12 of the two strata are going to be smaller than if you
13 treated it as one study. So I think it would come out in
14 the wash.

15 But, yeah, this was one when I was reading it. I
16 was sort of surprised you were still saying "suggestive"
17 for the reasons that Paul outlined. I mean the new --
18 this is a place where I think you'd have quite a lot of
19 strong new evidence. So maybe you should weigh it into
20 the Rubicon on this.

21 CHAIRPERSON FROINES: You may conclude that it is
22 still suggestive. I don't think Paul's saying you have to
23 come up with a conclusion. But I think that what he's
24 really saying is tell us what the criteria for your
25 decision is.

1 SUPERVISING TOXICOLOGIST MARTY: Well, there's,
2 you know, a certain amount of judgment involved on whether
3 you think there's enough studies that have been conducted
4 and how those -- how the positive studies pan out in terms
5 of are they better in terms of exposure estimation than
6 the studies that were not statistically significant? So
7 it really is a --

8 PANEL MEMBER GLANTZ: You know, but I think part
9 of it is that you should -- you know, that's one of the
10 things you get when you do the meta-analysis calculation,
11 is if you have -- you can have a series of small
12 non-significant studies, that when you pool them you would
13 find a significant elevation. And I think just looking at
14 the 1997 thing, I would be shocked if you went through
15 that exercise and found a significant elevation. But I
16 would think, again just eye-balling it, you may well if
17 you look at all of the studies today. But I mean I agree
18 with John. I mean I think you should also apply some
19 judgment here. But it's a much stronger -- certainly a
20 much stronger case than it was before.

21 PANEL MEMBER BLANC: You would -- I mean your
22 life would have been easier, I suppose, and I maybe
23 wouldn't even be hassling you as much if in 1997 they said
24 that those data were inconclusive. And maybe they sat
25 here and had a very long argument about that at the time.

1 And then you said, well, we're going from, you know,
2 inconclusive to at least suggestive. But it's hard. So
3 you may in fact be boxed into a corner a little bit by how
4 they did it. But it does on the face of it seem -- and if
5 you had some category that was between suggestive and
6 conclusive, okay, you could park it there. But this --

7 CHAIRPERSON FROINES: B-1, B-2.

8 PANEL MEMBER GLANTZ: I think we're now thinking
9 it --

10 PANEL MEMBER BLANC: Well, it's generic. I think
11 this is going to come up --

12 PANEL MEMBER GLANTZ: No, I agree with you.

13 CHAIRPERSON FROINES: This is going to come up
14 with -- this comes up all the time with other agencies and
15 this agency. I mean it's -- I mean it's one of the
16 reasons that people have tried to adopt Bayesian
17 approaches to decision making, right? So the short -- you
18 know, the standard in Greenland would say do a
19 meta-analysis. But somebody else in Boston would say do a
20 Bayesian approach to how you make decisions. And we're
21 sort of not saying that. But that's obviously an option.
22 So that it seems to me that the simpler thing to do would
23 be to make some kind of estimate based on the
24 meta-analysis.

25 SUPERVISING TOXICOLOGIST MARTY: Will do.

1 I just want to go through one of the better
2 studies, a couple of slides. Although we probably don't
3 need to do this. I could skip over to the comments if you
4 would like.

5 PANEL MEMBER BLANC: Yeah, I would.

6 --o0o--

7 CHAIRPERSON FROINES: It does mean that to the
8 degree that to the degree that we don't go through a
9 specific study, it is useful for the people who are
10 reading that chapter to make sure they're aware of those
11 specific studies.

12 SUPERVISING TOXICOLOGIST MARTY: Okay. We got a
13 number of comments on Chapter 3, primarily related to our
14 analysis of low birth weight. One of them is that there
15 are numerous factors linked to low birth weight, and this
16 presents a problem with confounding. And maternal smoking
17 is the biggest confounder.

18 And our response is that the effect is seen in
19 babies of non-smoking mothers exposed to ETS, not just
20 smoking mothers. We relied a little more heavily on
21 studies adjusting for many known confounders. And while
22 adjustment generally lowered the effect estimate, although
23 not always, they were still significant, even those that
24 got lowered.

25 And we also note a dose dependence of low birth

1 wait with maternal cotinine measured mid-pregnancy of
2 non-smoking mothers in Kharrazi. And then the consistency
3 of finding across numerous studies really supports
4 causality.

5 --o0o--

6 SUPERVISING TOXICOLOGIST MARTY: We got a comment
7 that while most studies did not reach statistical
8 significance for either decrements in birth weight, low
9 birth weight, as defined by 2500 grams or less, or small
10 for gestational age.

11 And our response is that of 22 risk estimates for
12 low birth weight, five were statistically significant, and
13 the majority were elevated. You can't just look at an
14 individual study absence of significance and then
15 individual study is not evidence of no effect. And we saw
16 dose dependence of both low birth weight and small for
17 gestational age related to maternal cotinine. So this is
18 a fairly good estimate of exposure. And then pool
19 estimates from meta-analyses indicate significant
20 decreases in birth weight.

21 --o0o--

22 SUPERVISING TOXICOLOGIST MARTY: We did get a
23 comment about confounding influence of adverse childhood
24 experiences, which the commenter shortened to ACES, and
25 that this was not measured. And the commenter cited

1 spousal abuse, lack of social support, and economic
2 prosperity as being risk factors for lowered fetal growth,
3 preterminal delivery and birth weight.

4 And our responses to the measures of SES are
5 meant to reflect, to some degree, societal stress. Most
6 of the studies that were conducted well considered SES.
7 And the effects were still significant after controlling
8 for SES. This may not control for every confounder of
9 course because there's no possible way of doing that. But
10 we don't think that the studies -- the database are
11 therefore -- you can't say there's effects of ETS.

12 --o0o--

13 SUPERVISING TOXICOLOGIST MARTY: And then,
14 finally, we got a comment on the attributable risk
15 calculation for low birth weight. This commenter said
16 that since smoking prevalence has dropped, then the low
17 birth weight should have also dropped, attributable to ETS
18 exposure. And they also said you should use the mean
19 serum cotinine from the latest NHANES to estimate the
20 number of people exposed to ETS in that attributable risk
21 calculations.

22 And our response is that -- well, first of all we
23 used survey data to look at the number of ETS exposed
24 individuals. But even if you try to use the mean
25 cotinine, that reflects both changes in numbers of the

1 people exposed as well as the amount of exposures. You're
2 not differentiating unexposed from exposed.

3 And that's essentially it for this chapter.

4 --o0o--

5 PANEL MEMBER BLANC: Would this chapter be an
6 example of where you would discount in the opposite
7 direction the direct smoking effect even for the well
8 established, and would not use that to be evidence of a
9 dose response, coming back to my earlier question, because
10 of the issue, for example, of maternal carbon monoxide?

11 SUPERVISING TOXICOLOGIST MARTY: We did not
12 discuss the effects of ETS very much in the context of
13 active smoking, other than to note that active smoking is
14 a confounder for all of these endpoints and that it was --
15 it's better to look at moms who didn't actively smoke
16 during pregnancy where that was possible. And some
17 studies actually we're able to do that.

18 We didn't talk about it in terms of dose
19 response. It's interesting, because who knows which
20 chemicals are the most responsible? You know, carbon
21 monoxide clearly is a candidate. Nicotine is a candidate.
22 But so are the PAH's for our intrauterine growth
23 retardation and so on. So it's -- you know, within that
24 context it's pretty hard to talk about active versus
25 passive.

1 And, Mark, I don't think we talked too much about
2 that in the chapter.

3 Okay. I think in the interests of getting
4 through the heavier-duty chapters, 6 and 7, where we
5 actually boosted a health outcome up to conclusive, that
6 we should go to those chapters now. Is that okay with the
7 Panel? And then we'll come back to 4,5, and 8 after 6 and
8 7.

9 --o0o--

10 SUPERVISING TOXICOLOGIST MARTY: Chapter 6 and 7
11 will be largely presented by Mark Miller.

12 CHAIRPERSON FROINES: I think that discussion was
13 very useful.

14 MR. MILLER: So chapter 6 is ETS and respiratory
15 disease. And you can see it's a substantially beefier
16 chapter than the last one.

17 And highlighted in yellow on the chart are the
18 two findings that went from suggestive to conclusive. And
19 those are asthma exacerbation in adults and asthma
20 induction in adults. As well as there are conclusive
21 findings on a number of areas that were unchanged from the
22 previous draft or previous 1997 document, which include
23 exacerbation of asthma in children, respiratory -- lower
24 respiratory infection, otitis media, sensory irritation
25 and annoyance, asthma induction in children, and

1 respiratory symptoms in children.

2 --o0o--

3 MR. MILLER: Starting with asthma exacerbation
4 among children, which in the previous document it was
5 concluded that ETS was a causal factor.

6 In this document that we're in, an additional 14
7 recent cross-sectional and cohort studies that were
8 reviewed, ETS exposure was assessed in these studies
9 varyingly by a questionnaire and some by cotinine and they
10 were associated with reduction in FEV1, increased report
11 of adverse symptoms, slower recovery from severe attacks.

12 It was noted that the cross-sectional studies
13 were limited by possible selection effects and that
14 smoking -- for example, smoking reduction by parents of
15 children with severe asthma might fall under this.

16 This would tend to bias toward the null any
17 observed risk estimate.

18 The longitudinal studies, which are less prone to
19 assert bias, were the most consistent studies with an
20 effect of ETS on childhood asthma.

21 --o0o--

22 MR. MILLER: Moving to adult asthma exacerbation,
23 which previously was listed as suggestive and upgraded to
24 a causal conclusive status.

25 A study by Dr. Blanc in 1999 looked at

1 respiratory work-associated disability and found that it
2 was increased by ETS; both a disability by an odds ratio
3 of 1.8, and symptomatic asthma, which was also increased,
4 though not statistically significantly so.

5 Another study by Dr. Eisner found serum cotinine
6 associated with pulmonary function decrements in
7 asthmatics. For example, an FEV run in women, a decrease
8 of 261 milliliters.

9 Dr. Kunzli found an ETS decreased pulmonary
10 function in asthmatic women and that there was a linear
11 dose response in a number of years and other factors.

12 Next slide.

13 --o0o--

14 MR. MILLER: Several -- at least two prospective
15 cohort studies were added.

16 A study by Sippel found asthma care events, in
17 other words needing to go into the doctor emergency room,
18 et cetera, were increased. Those exposed to ETS had 28
19 per 100 person-years compared to non-asthmatics with 10
20 per 100 person-years if they were not -- these are
21 asthmatics not exposed to ETS. Hospital care was more
22 than doubled.

23 Additional study by Dr. Eisner found -- and this
24 is one that we discussed earlier, where he did the
25 nicotine personal badges. And he found over a week's time

1 that there was an association with respiratory symptoms in
2 asthmatic adults.

3 The top number should be 0 to 0.05 micrograms per
4 meters cubed. And so -- which is considered the low
5 category. So there was non-exposed. There was the low
6 exposed category, which, for example, had a doubling of
7 bronchodilator; and the higher exposed category which had
8 an eight-fold statistically significant increase in
9 bronchodilator use.

10 PANEL MEMBER BLANC: Well, the study that I'm
11 most familiar with is obviously the one that I'm first
12 author of. And I think it's misplaced here. It's
13 relevant to the topic of ETS respiratory effects, but it's
14 not a study which is either focused on or directly
15 applicable to asthma exacerbation. So I don't think it
16 belongs --

17 MR. MILLER: Because it included any variety of
18 endpoints that would --

19 PANEL MEMBER BLANC: Well, the main endpoint is
20 workplace -- is changing your job because of breathing
21 difficulties on the job. And ETS was a risk factor for
22 that. But it wasn't looking at: "In asthmatics do you
23 get more exacerbations of asthma compared to people
24 without ETS?" So it's two steps removed from being able
25 to -- and there wasn't a stratified analysis presented

1 just among persons with asthma. And so I think that if
2 you have this sort of grab-bag section of other effects, I
3 would --

4 MR. MILLER: Yeah, respiratory illness, probably.

5 PANEL MEMBER BLANC: Or respiratory effects. So
6 you might want to expand that so that you have a place to
7 put studies.

8 And also I think it's worth noting that when we
9 did an analysis of data from other countries in the same
10 study, that analysis, although the primary thing we were
11 looking at which was workplace exposures to gases, dust
12 and fumes, were still associated with changing jobs. In
13 the larger European study where placing ETS exposure
14 wasn't related to changing jobs because it -- probably
15 because it included countries other than Sweden where, if
16 you left one job with ETS, you'd go to another job with
17 ETS. So it wouldn't be a reason why you would change
18 jobs. In Spain, for example.

19 So there's -- you know, even if I thought you
20 could put this here, because -- which I don't. I think
21 that you would need to put it side by side and put it in
22 the context of the negative study that, you know, used a
23 similar approach.

24 So I think it needs to come out of this table.
25 If you want to use it, you could use it in a sort of

1 different category, because it weakens your argument.

2 MR. MILLER: Uh-huh. Well, I think these other
3 studies that are presented here are directly looking at
4 asthma.

5 PANEL MEMBER BLANC: Yeah.

6 MR. MILLER: You know, there were a number of
7 studies that either fit into more than one kind of
8 category that we had or didn't quite fit into any exact
9 category. Yet we wanted to include them. But --

10 PANEL MEMBER BLANC: Now, I thought -- in the
11 extra studies that I sent you, was there one that was
12 relevant to this topic? Because it seemed to me that
13 there's been more -- it seems to me that the Jaakkola's
14 have something related to this, for example. But maybe
15 that's just asthma -- adult asthma incidents. I know this
16 is adult asthma exacerbation.

17 But this is one area in which -- since the most
18 recent study that you have is 2002, I believe that there's
19 more recent than that.

20 And that brings up another generic point that I
21 think is worthy of discussion here. I mean what struck me
22 about this chapter was that the -- systematically -- the
23 data from 2003 and 2002 were not mined as systematically.
24 Now, I know that this can't be a never-ending iterative
25 process. So, you know, there was a certain point where

1 you were writing this -- and you can't be expected to
2 include all things. I think that there are things that
3 came out in 2004, for example, after the time -- you
4 release this in December of 2003, so you can't be expected
5 to have all 2004 studies. And if you had to
6 never-endingly go back to the literature and keep
7 updating, the process would never end.

8 On the other hand, I think there are examples of
9 2004 studies that you're going to bring in because they're
10 so important and so relevant.

11 So as a panel member, it would help me to know
12 what makes you use a study that's after December 31st,
13 2003, and similarly that convinces me that before some
14 date in 2003 you feel confident that you adequately
15 searched the literature.

16 SUPERVISING TOXICOLOGIST MARTY: Well, I can tell
17 you that we -- while the document was out for public
18 comment and while we were responding to the comments, we
19 did go back and search PubNet and a few other databases
20 looking for studies that had been published that we
21 thought would add value to the chapter. And it's very
22 possible that, you know, we may have missed a few.

23 So we will definitely during this process go back
24 again and take another look at 2003 and 2004.

25 We did pick up some studies for other chapters

1 that were published in the meantime and put them in. So
2 that's why you see a few 2004's in here and some late
3 2003's.

4 PANEL MEMBER GLANTZ: I think it would helpful,
5 Paul, if you had some specifics things in mind to just
6 tell -- you know, send them the references.

7 PANEL MEMBER GLANTZ: I did that already.

8 SUPERVISING TOXICOLOGIST MARTY: He's done that.

9 PANEL MEMBER GLANTZ: Oh, ok.

10 PANEL MEMBER GLANTZ: But this is one in which,
11 you know, I just sort of had this existential sense that
12 there's other things out there.

13 SUPERVISING TOXICOLOGIST MARTY: We'll look.

14 PANEL MEMBER BLANC: Well, I'm happy look again
15 myself. That's why I asked if one of the four things I
16 sent you was relevant to this. I don't --

17 SUPERVISING TOXICOLOGIST MARTY: As my induction,
18 yes.

19 --o0o--

20 MR. MILLER: Moving on?

21 PANEL MEMBER BYUS: Yeah, actually just as an
22 aside, I found this discussion of the animal studies on
23 the postnatal development tobacco smoke -- they exposed
24 them -- was it OBA-specific IGE levels and they did these
25 studies. It was really very persuasive. I mean you could

1 include these things in various parts. There's a lot of
2 crossover.

3 SUPERVISING TOXICOLOGIST MARTY: Yes.

4 MR. MILLER: So I always thought why it was here
5 and not me --

6 SUPERVISING TOXICOLOGIST MARTY: Yeah, that was
7 part of our problem: Where do we put this stuff?

8 PANEL MEMBER BYUS: I know.

9 SUPERVISING TOXICOLOGIST MARTY: In fact, maybe
10 that one really is in the wrong place.

11 MR. MILLER: That really I think is in the wrong
12 place, because it doesn't even -- it isn't human. But --

13 SUPERVISING TOXICOLOGIST MARTY: All right. I'll
14 move it.

15 MR. MILLER: -- I would move it into the lung,
16 because it gives a good, you know, overview of how you may
17 sensitize the lung with environmental tobacco smoke
18 allergens in a producing eosinophilia, altering
19 lymphokines production. It's quite a -- at least from the
20 description here, it's quite a nice bit of data.

21 So that was all. Just move it.

22 SUPERVISING TOXICOLOGIST MARTY: Okay.

23 MR. MILLER: Continuing with adult asthma
24 exacerbation.

25 In a nested case-control study, Tarlo found

1 exacerbation of asthma with ETS exposure in the past year;
2 39 percent of the cases reported ETS exposure compared to
3 17 percent of controls, which was statistically
4 significant.

5 --o0o--

6 MR. MILLER: In summary, current studies provide
7 conclusive evidence that ETS exposure can cause asthma
8 exacerbation in adults. And although there were fewer
9 studies than in children, the data that we had appeared to
10 consistently link ETS exposure with poorer status among
11 asthmatic adults. And there was evidence in several
12 studies of dose response, and that the data on top of that
13 were quite consistent with the evidence in children, which
14 had already been conclusively linked.

15 PANEL MEMBER BLANC: And there are, by the way,
16 no controlled human exposure studies in those -- the last
17 interval that look at persons with underlying
18 hyperactivity who are exposed to secondhand smoke?

19 SUPERVISING TOXICOLOGIST MARTY: You mean
20 challenging them in a chamber study?

21 PANEL MEMBER BLANC: Yes.

22 SUPERVISING TOXICOLOGIST MARTY: Not that we
23 found.

24 PANEL MEMBER BYUS: Yeah, I was going to ask that
25 too.

1 MR. MILLER: The airport stuff -- they had an
2 airport smoking room --

3 SUPERVISING TOXICOLOGIST MARTY: That wasn't --

4 PANEL MEMBER GLANTZ: That was a
5 cardiovascular --

6 SUPERVISING TOXICOLOGIST MARTY: That was a
7 cardiovascular paper, and it wasn't controlled where they
8 had a specific concentration of PM or whatever.

9 We'll look to see if they're out there.

10 --o0o--

11 MR. MILLER: Respiratory illness in children has
12 had a recent meta-analysis which looked at the effects of
13 either or neither parent smoking on lower respiratory
14 infection in children under three years of age.

15 The meta-analysis result is this red figure at
16 the top. But there were 26 studies included. And you can
17 see the vast majority were positive and significantly so.

18 --o0o--

19 MR. MILLER: In summarizing lower respiratory
20 infection in children, there were 11 new studies which
21 strongly support the previous conclusion. And I think --
22 interestingly, there was a study that looked at annual
23 doctor consultations and the costs in Asia, and that there
24 was -- they were 14 percent higher with one smoker, 25
25 percent with two or more, and as well as various other

1 data.

2 I think we should move on here.

3 --o0o--

4 MR. MILLER: ETS and otis media --

5 PANEL MEMBER BLANC: Well, why does it say 6 in
6 your table and you say 11 in the slide?

7 MR. MILLER: In that -- that last table? Was 26
8 studies in the --

9 PANEL MEMBER BLANC: Eleven new studies.

10 MR. MILLER: Yeah.

11 PANEL MEMBER BLANC: And your table says six
12 additional studies.

13 MR. MILLER: I don't know which table we're
14 talking about.

15 SUPERVISING TOXICOLOGIST MARTY: I think he means
16 the table in the very beginning.

17 PANEL MEMBER BLANC: You're talking --

18 SUPERVISING TOXICOLOGIST MARTY: It does. It
19 says six.

20 PANEL MEMBER BLANC: -- about respiratory
21 illness, children.

22 MR. MILLER: I don't know. We'll have to look at
23 that.

24 SUPERVISING TOXICOLOGIST MARTY: Yeah. You know,
25 that could be one of the leftover things we never fixed.

1 As we kept adding stuff, we had to go back and find where
2 we said there were X number of new these type of study.
3 And we didn't -- clearly didn't catch them all.

4 MR. MILLER: We'll look.

5 PANEL MEMBER BLANC: And then I think that where
6 you have the zero in that table for 1997 studies, and then
7 a --

8 PANEL MEMBER HAMMOND: That was conclusive.

9 PANEL MEMBER BLANC: -- a footnote that says
10 there were no studies looked at because they accepted the
11 USEPA and Surgeon General's report. If you could at least
12 put in parentheses how many studies the Surgeon General's
13 report used, it would make it seem --

14 PANEL MEMBER HAMMOND: The USEPA was more recent.

15 PANEL MEMBER BLANC: Or whichever, make it seem
16 less bizarre.

17 PANEL MEMBER HAMMOND: Conclusive results on no
18 studies.

19 --o0o--

20 MR. MILLER: Otitis media previously was
21 conclusive and there were seven additional studies
22 reviewed, which are consistent, would then support the
23 previous conclusion. There was an estimate of the number
24 of office visits per year for otitis media in California,
25 children under three, attributable to ETS. And that has

1 decreased significantly primarily as a result of decreased
2 smoking.

3 --o0o--

4 MR. MILLER: ETS and asthma induction in
5 children. There were 37 recent studies. And on top of
6 that OEHHA has conducted a meta-analysis, which is
7 actually an update of the meta-analysis that was done for
8 the 1997 document. There were 85 studies that were
9 evaluated, over 460,000 children in 29 countries.

10 The pooled odds ratio for new onset asthma was
11 1.32 with tight confidence intervals. And that was based
12 on 29 well-controlled studies.

13 The relative risk of asthma onset among children
14 exposed to postnatal-only ETS -- that was an important
15 factor that had previously been difficult to pull out --
16 for the last five years was 1.22 and ten years was 1.42.

17 All preschool children appeared to be more at
18 risk. Older children exposed to ETS also appeared to be
19 at significant risk for new onset asthma. And the new
20 data analysis strongly support the previous conclusion
21 that ETS exposure is causally associated with new onset
22 asthma in children.

23 PANEL MEMBER BLANC: And this is again another
24 place where your first table doesn't bear any resemblance
25 in numbers. So do double check what you're --

1 MR. MILLER: Well, that certainly is an area that
2 we had continued to update right up to the last --

3 CHAIRPERSON FROINES: Paul, say that again. I
4 didn't understand what you were saying.

5 PANEL MEMBER BLANC: Their table says there are
6 28 additional ease in this update. Actually you said 37
7 recent studies. But I think you took from the wrong
8 column. But even so, there was nothing you had that was
9 like a 28.

10 And, again, this is another -- we talked in a
11 previous section about some way of giving due credit to
12 meta-analysis that have been published, you know,
13 systematically throughout the review. If you can -- you
14 know, these table, I don't -- it gets a little
15 complicated, but there must be some way of putting them in
16 prominent --

17 MR. MILLER: Adding those in?

18 PANEL MEMBER BLANC: Yeah.

19 Another column of meta-analysis maybe, yeah.

20 MR MILLER: Adult onset asthma, start by looking
21 at dose-response relationships. There were studies -- the
22 number of studies that demonstrated dose response
23 relationships between their studies, including looking at
24 total duration of ETS exposure, number of smokers in the
25 environment, duration of exposure to smokers, duration of

1 working with a smoker, measured nicotine levels, and index
2 of intensity and duration of exposure. Obviously with
3 many different metrics and hard to absolutely compare
4 sometimes between these.

5 Next slide.

6 PANEL MEMBER BLANC: Okay. Now, wait a second.
7 Not so fast.

8 Another example of a study that I thought was in
9 the wrong place -- not that it's not relevant somehow in
10 this chapter -- is the -- this Eisner nicotine level,
11 isn't that the same study you were quoting previously,
12 which was only done among persons with asthma? Is this
13 some other study? Ice ice mark ice err

14 SUPERVISING TOXICOLOGIST MARTY: This is Mark
15 Eisner, who did the study.

16 PANEL MEMBER BLANC: So that should not be in
17 this section. It was --

18 MR. MILLER: Should be in the other section.

19 PANEL MEMBER BLANC: It was in the other section,
20 which is where it should be. But it should not be cited
21 here.

22 MR. MILLER: Okay. We'll talk to Dr. Eisner
23 about that.

24 Next slide.

25 --o0o--

1 MR. MILLER: The consistency of study findings
2 supports a causal association. Associations were found in
3 different populations that range from clinical to
4 population-based studies. And they were across many
5 different countries. There were consistent findings in a
6 variety of study designs including cross-sectional case
7 control and cohort studies, and in different environments
8 such as home and work exposures.

9 --o0o--

10 MR. MILLER: Biologic plausibility is supported
11 by studies of adults finding a small but significant
12 deleterious effect of ETS on pulmonary function, some
13 examples of which are there.

14 ETS contains potent respiratory irritants that
15 adversely affect bronchial smooth muscle tone and airway
16 inflammation. So this isn't surprising.

17 Coherence is supported by associated and related
18 health outcomes, such as chronic respiratory disease,
19 respiratory symptoms such as wheezing, cough, et cetera.

20 SUPERVISING TOXICOLOGIST MARTY: I might add --

21 CHAIRPERSON FROINES: So could you go back to
22 that.

23 MR. MILLER: Okay. I'm going to go slow.

24 CHAIRPERSON FROINES: No, go ahead and --

25 PANEL MEMBER BYUS: I just have a question about

1 asthma in general. I mean are -- so you're saying here
2 adult new onset asthma. So are we assuming that if people
3 were not exposed -- that these people would never get
4 asthma if they were not exposed to ETS?

5 PANEL MEMBER BLANC: We'll, that's the --

6 CHAIRPERSON FROINES: I mean that's kind of the
7 question here.

8 PANEL MEMBER BLANC: That is -- that's what
9 differentiates this from studying asthma exacerbation --

10 PANEL MEMBER BYUS: And that's what you're
11 saying. So in other words --

12 PANEL MEMBER BLANC: That's what the studies --

13 PANEL MEMBER BYUS: They would not be -- they
14 would never be asthmatic if it wasn't for ETS?

15 PANEL MEMBER BLANC: Well, let me -- I can
16 answer your question in a different way. You could
17 calculate an attributable risk fraction for asthma based
18 on these studies; because it's a relative risk for an odds
19 ratio of asthma, and the presumption is without this
20 factor you would not have asthma -- you would not have
21 gotten asthma --

22 MR. MILLER: You mean they attempted --

23 PANEL MEMBER BLANC: -- from an epidemiologic
24 point of view.

25 MR. MILLER: Yeah, the attempt is to take two

1 comparable groups of people, and the difference is the ETS
2 exposure.

3 PANEL MEMBER BYUS: But in terms of etiology --
4 I'm asking just in terms of the etiology of what we know
5 about asthma as a disease -- is that a likely conclusion?

6 PANEL MEMBER BLANC: Yes, because I think the one
7 issue of biological plausibility that should be alluded to
8 is the -- there are two issues related to cigarette smoke.
9 One would be the growing body of evidence which indicates
10 that chemical irritants can induce asthma. So I think
11 that needs to be mentioned in your discussion of
12 biological plausibility with, you know, one or two
13 citations of reviews of irritant-induced asthma.

14 And, secondly, there's a growing body of evidence
15 which also shows that cigarette smoke can act -- and other
16 inhalants can act as adjuvants for sensitization. So it
17 could be a mechanism towards sensitization. But what --

18 PANEL MEMBER BYUS: That's an explanation, right.

19 PANEL MEMBER BLANC: But that's not the main
20 explanation. The more straightforward --

21 CHAIRPERSON FROINES: Who can act as an adjuvant
22 for sensitization?

23 PANEL MEMBER BLANC: Irritants.

24 But irritants without invoking sensitization are
25 associated with adult onset asthma.

1 But in that vein -- just before you asked your
2 question, John -- is this a situation in which your
3 apriori belief would be that an association between direct
4 cigarette smoking and asthma onset in adulthood would be
5 supportive of your argument?

6 SUPERVISING TOXICOLOGIST MARTY: I would -- yes,
7 I would think so, yes.

8 PANEL MEMBER BLANC: So why is it missing from
9 your argument here? Why isn't this in particular a
10 situation in which you would want to address that
11 literature? Now, that literature has certain problems, I
12 grant you. Because people who develop respiratory disease
13 in adulthood who are smokers tend to get labeled as having
14 COPD and not labeled as having asthma. So there's a
15 certain diagnostic bias.

16 But, for example, there is an article that just
17 came out from the Jaakkola's in the last month that is on
18 adult onset asthma in association with direct smoking.
19 And it has a good discussion of, you know, the
20 epidemiology of the subject. And I think that -- doesn't
21 one of the Surgeon General's reports talk about direct
22 smoking and asthma?

23 SUPERVISING TOXICOLOGIST MARTY: I think so, yes.

24 PANEL MEMBER BLANC: So I think that that should
25 definitely be invoked here. Because if direct smoking

1 didn't cause asthma, it would be hard to imagine how ETS
2 could cause asthma.

3 SUPERVISING TOXICOLOGIST MARTY: Exactly.

4 PANEL MEMBER BLANC: Whereas some of these other
5 arguments I could buy about not linear or even anti-linear
6 responses, but not here.

7 CHAIRPERSON FROINES: I just had one comment,
8 which could open Pandora's Box with my friend Blanc. So I
9 will be cautious about it. But I don't think -- I think
10 that as a matter of mechanism, we're not really dealing
11 with mechanism in general here. And so, whereas, I agree
12 that there is certainly literature on respiratory
13 irritants in relation to asthma, I don't think that is the
14 only substances that are capable of producing asthma.

15 SUPERVISING TOXICOLOGIST MARTY: Absolutely.

16 CHAIRPERSON FROINES: And so making that
17 statement seems to imply to me that there are other things
18 that I think are important that Blanc may not.

19 (Laughter.)

20 CHAIRPERSON FROINES: And so I think that we need
21 to say respiratory irritants and other agents or something
22 so that I -- that I have my piece of the action in terms
23 of this --

24 SUPERVISING TOXICOLOGIST MARTY: Actually I had
25 asked the staff to put respiratory irritants in

1 immunotoxicants, thinking back to the diesel literature
2 and looking at PAH's and how they can moderate the immune
3 system.

4 CHAIRPERSON FROINES: Well, we'd like -- we of
5 course like things like to generate reactive oxygen. And
6 it's not only --

7 PANEL MEMBER BLANC: Don't you want to say
8 something about mytroso -- polycyclic mitroso in --

9 CHAIRPERSON FROINES: No.

10 (Laughter.)

11 CHAIRPERSON FROINES: But I would say
12 something --

13 PANEL MEMBER BLANC: Because if I don't get
14 through one meeting without you talking about --

15 CHAIRPERSON FROINES: But I would say something
16 about quinones.

17 PANEL MEMBER BYUS: But it seems almost as good,
18 right?

19 CHAIRPERSON FROINES: I mean I wouldn't want to
20 leave the room without having said the word "quinone" once
21 during this discussion.

22 PANEL MEMBER GLANTZ: No jokes now.

23 CHAIRPERSON FROINES: Oh, that's right, no jokes.

24 This was meant as a joke, not entirely.

25 (Laughter.)

1 CHAIRPERSON FROINES: Let's go ahead. The
2 point's made.

3 --o0o--

4 MR. MILLER: Okay. Several studies directly
5 support the impact of ETS exposure on incident adult
6 asthma. And other studies have prospectively examined the
7 relationship between ETS exposure and incident wheezing.

8 --o0o--

9 MR. MILLER: So for once we go over this?

10 SUPERVISING TOXICOLOGIST MARTY: I think we can
11 skip it.

12 MR. MILLER: We'll pass it.

13 --o0o--

14 MR. MILLER: This is the prime study. Just to
15 remark that to take a look at the information on
16 Jaakkola's 2003 study. That is probably the gold standard
17 as far as what's been published to date.

18 --o0o--

19 MR. MILLER: So looking at the variety of studies
20 that were reviewed in the literature that we looked at in
21 this document, there are -- as well as a few of the older
22 studies. Here are from Cohort Case Control and
23 Cross-sectional Studies the spectrum of associations. We
24 see that most of the studies are positive, nearly all of
25 them; and many of them significantly so.

1 Next.

2 --o0o--

3 MR. MILLER: So in summary, there were nine
4 recent studies of variety of designs, eight of which
5 showed significantly increased risk for adult onset asthma
6 in one or both genders, ranging from odds ratios of 1.14
7 to 4.8.

8 ETS exposure in childhood increased the risk of
9 adult asthma in several studies that looked at that.

10 PANEL MEMBER BLANC: Yeah, that was an area of
11 this document that was -- I started to get a little lost
12 in. And it made me wonder if -- you know, you were using
13 adolescents as children when it served your purposes and
14 using adolescents as adults when it served your purposes.
15 And I didn't -- I found that troublesome in the
16 document -- in this chapter. I can't cite you chapter and
17 verse. Actually I'm citing you chapter but not verse
18 where this has happened. And then there was this business
19 about so and so was exposed in childhood and then they --
20 it's seemed like a somewhat different issue.

21 MR. MILLER: Well, at least one study had the
22 onset of the whole -- where it was in secondary school,
23 followed them I think to page 22. And so it crosses all
24 boundaries.

25 PANEL MEMBER BLANC: So is there -- I mean I

1 don't know whether you want a separate discussion about
2 adolescence and second-hand smoke and respiratory effects,
3 whether that's -- whether there just aren't enough data to
4 allow you to do that, or in the miscellaneous category.
5 But, anyway, that was one study that I just seemed to
6 muddy the waters more than clarify for me.

7 MR. MILLER: I mean I looked at that as -- I mean
8 where you want to cross the boundary -- you know, in the
9 childhood stuff, I think we basically looked at 12 as --
10 you know, kind of this early childhood. Then there's a
11 break in the early childhood and then the later early
12 childhood. And --

13 PANEL MEMBER BLANC: But in asthma it's a
14 particularly important period with a lot of different
15 things going on because it's when the ratio of male to
16 female asthma switches, it's when smoking is initiated,
17 it's therefore when ETS exposure among peers is initiated,
18 you know. Children who are -- adolescents who come into
19 adolescents as smokers -- I mean as asthmatics actually
20 tend to start smoking as much as non-asthmatics. But
21 adolescents who get asthma in adolescents tend not to. I
22 mean there's a lot of weird, you know, temporal
23 complicating factors.

24 A general, I would say, that if your argument
25 isn't substantive, we can -- by taking out that study, I

1 would put it somewhere else in this chapter.

2 --o0o--

3 MR. MILLER: Looking at lung growth and
4 development. There were additional seven studies. And it
5 really was consistent with the previous information.

6 --o0o--

7 MR. MILLER: There was some difference in FEV 1
8 between children of smokers and non-smokers looked at in
9 this study, with decreases in nearly all the -- this is a
10 meta-analysis from Cook in nearly all the studies that
11 they've looked at.

12 --o0o--

13 MR. MILLER: Move to responses to comments. The
14 American Lung Association and Lorillard both had a comment
15 that more or less read that the review of the data in the
16 draft report lead us to believe that the link to asthma
17 induction in adults requires further scientific study to
18 merit conclusive findings.

19 And our response was that the evidence satisfies
20 the Hill criteria that exposure response by measures of
21 daily exposure and a number of other ways of looking at
22 that was shown.

23 PANEL MEMBER BLANC: I think the last name is
24 Bradford-Hill. Bradford is not his first name. It's
25 Austin Bradford-Hill, something like that, just so you

1 know.

2 MR. MILLER: The Bradford-Hill criteria.

3 PANEL MEMBER BLANC: Thank you.

4 MR. MILLER: Temporal relationship was showing
5 that asthma follows ETS exposure. There was consistency
6 between studies found in a variety of different settings
7 and study types. There was biologic plausibility. And
8 that the recent population-based-incident asthma study by
9 Jaakkola distinguished between incident and between
10 previous and new onset asthma in adults, as well as being
11 a very strong study in other measures.

12 --o0o--

13 MR. MILLER: The additional comment from the
14 American Lung Association --

15 PANEL MEMBER HAMMOND: Excuse me. I'm sorry.
16 What's the difference between incident and new
17 onset?

18 MR. MILLER: That changed the wording there.

19 PANEL MEMBER HAMMOND: You said something
20 different. I just -- yeah, okay.

21 All right. Fine.

22 MR. MILLER: The point was that in the past
23 there's been with a number of the studies an issue about,
24 you know, are you really looking at new onset in adult as
25 opposed to somebody who had it as a child and didn't have

1 it for a period of time and now it's diagnosed again. And
2 Jaakkola's able to do that because of their -- they have
3 this national data of both, you know, as far as
4 medications that are paid for and as well as they were
5 able to survey all clinic visits and that sort of thing.

6 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

7 SALMON: Scandinavia effect.

8 (Laughter.)

9 MR. MILLER: I have some additional from the
10 American Lung Association. And they said it's not as
11 clear as to whether post-natal ETS exposure triggers an
12 attack in a child who is pre-disposed to asthma or induces
13 the first attack of an existing condition. More or less
14 that same thing we were talking about in adults, but a
15 little more difficult to understand what the question is.

16 Well, at least in several studies that were
17 evaluated I think there were four that fit into this being
18 able to look at that question, that were looked at in the
19 meta-analysis that we had done. But here's an example of
20 one of those, where Mannino classified the children by
21 their cotinine levels and then specifically was able to
22 pull out those that were positive PNS, in other words that
23 was prenatal smoking by the mother, on the top line. And
24 then the next line is negative PNS, so there was no
25 prenatal smoking. So that their exposure was postnatal.

1 And you can see that there was significant elevation in
2 current asthma in children who were not exposed to
3 prenatal smoke, but were exposed to postnatal smoke.

4 PANEL MEMBER BLANC: Prenatal maternal smoke?

5 MR. MILLER: Prenatal maternal smoking.

6 Yeah, that was the primary issue, prenatal
7 maternal smoking.

8 In addition, we felt that it was probably a
9 semantic issue as to whether asthma after postnatal ETS on
10 top of some in-utero exposure can be said to be induced
11 asthma or an uncovering of a preexisting tendency that
12 even though postnatal exposure leads to increased risk
13 among those already primed by prenatal exposure, we would
14 still consider that the onset of asthma induced by
15 environmental tobacco smoke.

16 --o0o--

17 MR. MILLER: An additional comment from
18 Lorillard. Analyses must account for obesity, infection,
19 atopy, and other potential risk factors, as well as
20 potential reporting, misclassification and biases.

21 Our response is that there's no evidence that
22 unmodeled confounding explains the ETS-asthma association.
23 And in the studies reported, after adjustment for multiple
24 confounders, the evidence still points to a role of ETS in
25 asthma causation.

1 Bias is always a concern. But we did not feel
2 that that was adequate to suffice to explain the results
3 we see.

4 --o0o--

5 MR. MILLER: There were -- Lorillard again --
6 nine new studies, are inadequate to conclude causality.
7 Causality can't be determined by cross-sectional studies.
8 The finding of causality was based on numerous studies of
9 different designs, not just cross-sectional studies.

10 Additionally, self-diagnosis of asthma is
11 unreliable. There's no biochemical determination of
12 exposure.

13 The use of self-report and questionnaires is a
14 standard technique which has been well validated in
15 numerous studies. But, in addition, the recent study by
16 Jaakkola used the clinical diagnosis and pulmonary
17 function testings and showed association between ETS and
18 asthma.

19 Recall bias can't be eliminated from
20 retrospective studies. The results from the retrospective
21 studies agree with those from prospective studies.

22 --o0o--

23 SUPERVISING TOXICOLOGIST MARTY: That's it for
24 Chapter 6. And we are at 1:22.

25 PANEL MEMBER BLANC: All right. So now I have

1 some substantive comments.

2 I think that this chapter needs to be
3 reorganized. I think for some reason you've locked
4 yourself into whatever order it was that the last document
5 had perhaps. But it would be far more logical to proceed
6 through the childhood endpoints you're looking at and then
7 go to the adult endpoints, rather than jump back and
8 forth, childhood asthma, adult asthma, childhood, de novo
9 asthma, adult, de novo asthma, childhood -- whatever.

10 First of all, it makes this lung development
11 thing sort of come out in the middle of nowhere, where it
12 doesn't belong. So I would start with lung development
13 since that's sort of pre-childhood. Then I'd do all your
14 childhood stuff and then I'd do all your adult stuff. And
15 I think you'd find that it would be more logical and
16 easier to follow for the reader. And it may make the
17 choices of where you put certain of these papers somewhat
18 easier.

19 I also think that the category that you call
20 respiratory symptoms should be respiratory symptoms and
21 other effects, to allow yourself a place where you could
22 put lung function decrements that aren't defined by a
23 diagnostic category or other things.

24 And I'd leave it till you think about this
25 adolescent question.

1 MR. MILLER: We should specifically try to look
2 at which studies have parts of it which address
3 adolescents?

4 PANEL MEMBER BLANC: Yeah. So I -- and then of
5 course recheck your -- check your numbers. And then on
6 certain of these things I would -- be hyper-vigilant about
7 the literature where it seems like I would have expected
8 more than before.

9 I guess another question is -- you know, if you'd
10 just look at -- for many of these things of course the
11 conclusive to conclusive is the -- or it's staying
12 suggestive-suggestive. And it's only a couple things
13 where you really have a step up in your level of
14 causality.

15 And this, again, is a generic comment. Do you
16 throughout the document use the same approach for those
17 category shifts? Are you consistent? Is there a little
18 mantra that you do every time you're jumping from
19 suggestive to conclusive where that's where you do the
20 Bradford-Hill drill and in other places you don't do the
21 Bradford-Hill drill? Is that what you're --

22 SUPERVISING TOXICOLOGIST MARTY: We did do that
23 in this case. Where it went to conclusive we did the
24 Bradford-Hill --

25 PANEL MEMBER BLANC: And you do that throughout

1 the document?

2 SUPERVISING TOXICOLOGIST MARTY: -- discussion
3 within the document.

4 There's only two places where it jumped from
5 suggestive to conclusive.

6 PANEL MEMBER BLANC: Well, no. Here there's two
7 separate categories. There's asthma exacerbation in
8 adult --

9 SUPERVISING TOXICOLOGIST MARTY: -- and
10 induction.

11 PANEL MEMBER BLANC: -- and asthma.

12 So you go through the Bradford-Hill twice -- two
13 separate times at the conclusion of each subsection?

14 MR. MILLER: We just did it with induction.

15 SUPERVISING TOXICOLOGIST MARTY: We just did it
16 with the induction because we thought that was more hairy.

17 PANEL MEMBER BLANC: Okay. So that's exactly my
18 point. You're inconsistent.

19 I actually would suggest that for every place
20 where you go from suggestive to conclusive and you've made
21 that leap, that you go through systematically why you did
22 it using a modified Bradford-Hill approach to the extent
23 that it's -- rather than simply responding to these
24 comments in a letter, which is not -- you know, which --
25 or printed comments, which are not actually in the body of

1 the report. And that goes back to our question about why
2 did -- when you had nine studies all in the same direction
3 for the, you know, other effect was that still only just
4 more suggestive?

5 I'm not saying that when you do the reverse you
6 have to go through that. When you don't make the leap you
7 have to suddenly say why it is you don't. But when you
8 do, I think you should consistently.

9 MR. MILLER: I think the only incidence would --
10 the only the point at which we didn't do that is asthma
11 exacerbation in adults.

12 SUPERVISING TOXICOLOGIST MARTY: Well, the two
13 places we did it were breast cancer and asthma induction
14 in adults. Those were the two places we did that.

15 PANEL MEMBER BLANC: Well, for example, if in the
16 end you decide that you're going to make the leap on --

17 SUPERVISING TOXICOLOGIST MARTY: -- preterm
18 delivery --

19 PANEL MEMBER BLANC: -- preterm, and then the
20 other stuff I think I sent you, the lengthy...

21 CHAIRPERSON FROINES: I think that some of what
22 Paul is saying also could be added -- some shortened
23 version could be added to the chapter summary and
24 conclusions, so you'd know exactly where you can find the
25 information.

1 I should tell you, by the way, that your table of
2 contents is not accurate. According to this, the chapter
3 summary and conclusions is 6-94. It's actually on 6-109.

4 SUPERVISING TOXICOLOGIST MARTY: How could that
5 be? We did that one in Word.

6 MR. MILLER: A computer glitch. That was
7 generated by the --

8 SUPERVISING TOXICOLOGIST MARTY: It should have
9 been created -- it was generated by Word.

10 PANEL MEMBER GLANTZ: This is why I still use
11 Word Perfect. It doesn't have these problems.

12 CHAIRPERSON FROINES: I have 6-109.
13 So it's on 6-109, 6-110, 6-111 in my version.

14 PANEL MEMBER BLANC: Do you have SRP version or
15 the --

16 CHAIRPERSON FROINES: Yes, I do.

17 PANEL MEMBER BLANC: -- or the early-bird
18 version?

19 CHAIRPERSON FROINES: It's October 2004.

20 Anyway --

21 SUPERVISING TOXICOLOGIST MARTY: It might be a
22 glitch with going to PDF also.

23 CHAIRPERSON FROINES: Let's not take any more
24 time on this.

25 SUPERVISING TOXICOLOGIST MARTY: Okay.

1 CHAIRPERSON FROINES: We can come back to this.
2 But I still find that the chapter summary and conclusions
3 would deserve further look, and let's just put it that way
4 for now, in terms of its accuracy.

5 I'm very interested in having a document that a
6 large group of readers can actually find conclusions very
7 clearly stated. It's such a massive document.

8 PANEL MEMBER BLANC: Well, one question -- maybe
9 this is more a question for John. If you go to page 6-110
10 and 111 as a prototypical chapter summary and conclusions,
11 it's a very long chapter. One of the things that they
12 have done is in some places put references in again
13 parenthetically in your time summary. And, for example,
14 that's not a place where I would necessarily be looking
15 for you to recite the reference citations that you've
16 cited, you know, five pages ago in the specifically
17 things. Although maybe that's my own editorial quirk.

18 I mean I would rather have you do the summary and
19 say, "As shown in Section 3, through 15 studies" blah,
20 blah, blah, "as shown in Section," you know, X, blah blah
21 blah. But I don't -- why do you have to reiterate all of
22 these references in each of your -- because then you're
23 citing some references but not the others, so these are
24 the references you really, really like.

25 (Laughter.)

1 PANEL MEMBER BLANC: You know, what's the
2 implication? It makes it -- well, anyway.

3 SUPERVISING TOXICOLOGIST MARTY: We can take them
4 out. That's fine.

5 PANEL MEMBER BLANC: You certainly don't have
6 references in your executive summary, do you, of the whole
7 thing?

8 CHAIRPERSON FROINES: Well, Paul knows that I
9 also think that -- and he and I actually disagree on this
10 a little bit -- that citing studies that were your weight
11 of evidence seems to me to be a reasonable conclusory
12 approach. And he disagrees with that. So we have a
13 slight difference of opinion.

14 I don't know what -- I do think that this could
15 be broken out more so the conclusions are very clearly
16 defined according to endpoints. And I think that Paul
17 argued earlier with Charlie and me that we don't really
18 need to have that list of the studies that were positive,
19 because then it raises the question of "what did you leave
20 out" was his concern.

21 So I think the two of them, judging from
22 Charlie's nodding his head, that we probably don't need
23 them. But we do need, therefore, a very careful statement
24 about what the conclusions were in terms of...

25 PANEL MEMBER BLANC: I would certainly emphasize

1 in your conclusions of each chapter at the outset of the
2 conclusions, as this chapter has shown, we have raised the
3 status of two health outcomes that were previously
4 considered suggestive to the level of conclusive. These
5 are "exacerbation of adult asthma" and "new onset adult
6 asthma".

7 For each of the other -- for none of the other --
8 for all the other endpoints, you know, the findings
9 were -- or new studies were overall supportive of the
10 original conclusions. And in two cases, findings which
11 were suggestive are strengthened, although not -- you
12 know, we have not determined that they're conclusive.

13 I mean, that -- you know, march the reader
14 through what you think matters in the chapter.

15 MR. MILLER: Yeah, you'd like somebody to be able
16 to go to the conclusion and use that as -- there's kind a
17 summary of what was in there.

18 PANEL MEMBER BLANC: So that when you did an
19 executive summary, what you'd really do is just pull these
20 out and, you know, make them coherent.

21 CHAIRPERSON FROINES: The other thing is, I think
22 in -- and I think this is true with breast cancer, is that
23 it's almost as though your conclusions you rely on -- and
24 it's in here -- you basically come to the end and you're
25 ready for your conclusions, and in citing your conclusions

1 you rely on the meta-analysis as the statement of reasons.
2 And I actually don't think that the meta-analysis is the
3 basis of your conclusion. I think the meta-analysis is
4 one of the elements that lead to your conclusions. And I
5 think this goes back earlier to the earlier question about
6 counting meta-analysis vis-a-vis individual studies.

7 And so this -- you keep going through
8 meta-analysis in your conclusions as though they were the
9 defining feature. And I'm not sure you really mean that.
10 If you mean, then say it. But I'm not sure that's what
11 you really mean. Or I'm not sure that's -- because people
12 who hate meta-analyses, of which there are large numbers,
13 are not necessarily going to be convinced by that level of
14 argument.

15 I mean are you saying that positive meta-analysis
16 is the base of your conclusion? No, you're not really
17 saying that, are you?

18 SUPERVISING TOXICOLOGIST MARTY: It strengthens
19 it.

20 CHAIRPERSON FROINES: It strengthens it. So that
21 it seems to me you need a slightly different context.
22 Because this reads as though it's a causal statement -- I
23 mean it's a defining statement.

24 PANEL MEMBER BLANC: In fact, how -- Stan, maybe
25 this is a question for you. How does a positive

1 meta-analysis fit into the causal argument in the
2 Bradford-Hill view? Is it evidence of strength of
3 association or is it evidence of consistency of the
4 association?

5 PANEL MEMBER GLANTZ: I think both. I mean the
6 stronger the association that you have -- or the larger
7 the magnitude of the association that you -- or the larger
8 the magnitude of the effect that you see, the easier it is
9 to see. And I mean the meta-analysis is just -- I mean is
10 just a way of saying if you take the studies together and
11 sort of average them, what do you come up with on average
12 weighting them by study size essentially?

13 So I think finding a significant elevation in a
14 meta-analysis when you have a whole bunch of small studies
15 is just the way of looking at the epi information all at
16 once and coming up with a summary statistic. And, you
17 know -- so if you find a significant elevation in a
18 meta-analysis, that I think strengthens your case. But
19 then I think, as they did in the breast cancer in
20 particular and then cardiovascular disease also, to then
21 look not just at the epi-studies, but at the toxicology
22 and at the experimental work and the mechanistic studies
23 and things like that. I mean that is what I view as a
24 weight of evidence.

25 You know, do all the -- I mean when I look and

1 say cardiovascular disease, the thing which is to me most
2 compelling is that if you -- you can look at a whole lot
3 of different kinds of evidence and they all point to the
4 same conclusion. And, you know, there's no one level of
5 evidence which is perfect. I mean if you talk about an
6 epi-study, it's always messy. There's always something
7 wrong with all epi-studies. But the advantage of an
8 epi-study is it's in the real world, you know.

9 But then the other extreme, if you go to a
10 molecular biology or cellular biology studies that show
11 toxic effects of the smoke or something in the smoke, then
12 that is very supportive, but it's also a tremendously
13 artificial environment.

14 And so, you know, I think what you want to do is
15 step back and look at all of these different kinds of
16 evidence and just see how consistent is the picture that
17 they paint.

18 CHAIRPERSON FROINES: Let me just make one
19 argument about that.

20 I think that this artificial environment that you
21 just said I really would quarrel with, because I think
22 that comes from a bunch of people who make lists of
23 chemicals that are found in tobacco smoke, and I would
24 agree with you there, if you say butadiene, formaldehyde,
25 Benzene. And people who don't know anything about

1 chemistry often list chemicals and make a case as though
2 that was sufficient.

3 However, the issue as far as I'm concerned is:
4 Does the chemistry of those compounds support a
5 mechanistic view of the health outcomes? And that
6 actually I take as being a serious -- a real contribution.

7 PANEL MEMBER GLANTZ: Oh, no, I --

8 CHAIRPERSON FROINES: Just listing toxic
9 chemicals is fine and well and good. But it's not
10 sufficient because it doesn't go to the chemistry of --
11 and the basically chemical mechanism of these effects.

12 PANEL MEMBER GLANTZ: Oh, no, I -- that wasn't
13 what I was trying to say. I think when you -- and I agree
14 with what you said. But I think that when you do -- you
15 know, for example, some of the work we've done where
16 you'll take an experimental animal and expose them to
17 secondhand smoke in a very highly controlled way, you
18 know, you can be more confident about the effect -- you
19 induced an effect in an experiment, but it's not a
20 normal kind -- it's not like a human being walking around,
21 living day to day.

22 And so to the extent that you constrained the
23 environment in an experimental situation, which
24 strengthens your experimental conclusions, it I think by
25 its very nature takes you more distant from reality in

1 terms of what people walking around are actually -- you
2 know, like if you're doing an experiment exposing rats to
3 secondhand smoke, they're not out on the street breathing
4 diesel exhaust, you know.

5 CHAIRPERSON FROINES: Kathy would --

6 PANEL MEMBER GLANTZ: Kathy would be measuring --

7 CHAIRPERSON FROINES: I want to give her a chance
8 before I get back and --

9 PANEL MEMBER HAMMOND: Yeah. And I agree with
10 both of your points there.

11 But going back to Paul's question about the
12 meta-analysis. I think disagree with Stan on that. I
13 think a meta-analysis is not going to give you a stronger
14 effect or a higher, you know, relative risk. You know,
15 usually it's going to be something in the middle. But
16 rather what it gives you is it eliminates the likelihood
17 that chance was the underlying reason for the result --
18 the positive result you saw. And so --

19 PANEL MEMBER GLANTZ: Well, no, what I -- I'm not
20 just going -- because you're not disagreeing with -- I
21 wasn't clear.

22 PANEL MEMBER BLANC: Heaven forbid.

23 PANEL MEMBER GLANTZ: What I was -- I was talking
24 about two different things.

25 Okay. One of them is in the meta-analyses you

1 can increase the precision of your estimate --

2 PANEL MEMBER HAMMOND: Yes.

3 PANEL MEMBER GLANTZ: -- which is what Kathy is
4 saying.

5 The other thing I was saying is that if in
6 doing -- if in doing the meta-analysis, the higher the
7 overall estimate of the risk that the meta-analysis
8 yields, the more confident you could be --

9 PANEL MEMBER HAMMOND: But that's true of the
10 meta-analysis of any single study.

11 PANEL MEMBER GLANTZ: That's true.

12 PANEL MEMBER HAMMOND: But I mean in terms of I
13 think the contribution the meta-analysis brings -- the
14 unique contribution in the Bradford-Hill is to narrow the
15 confidence interval.

16 PANEL MEMBER GLANTZ: Yes, I agree with that.

17 CHAIRPERSON FROINES: I think Paul actually had a
18 hidden position when he asked that question. Because I
19 think he was --

20 (Laughter.)

21 CHAIRPERSON FROINES: -- really saying that he
22 thinks it strengthens the consistency argument, but not
23 necessarily strengthens the association.

24 PANEL MEMBER BLANC: It actually was not a -- it
25 was not a rhetorical question, because as I think about

1 it, I'm not really -- I'm still not really clear. And
2 maybe one of the problems with meta-analysis or the
3 contradiction of meta-analysis is that we put a lot of
4 weight in them, that we find them very reassuring. We
5 don't -- they don't drive everything, but we're very --
6 we're very reassured when a meta-analysis yields results
7 that are consistent.

8 But a meta-analysis is not so easy to pigeonhole
9 in the Bradford-Hill way of divvying up the world, because
10 in some senses it's an issue related to consistency and in
11 some ways it's related a bit to strength of association.
12 But it doesn't --

13 PANEL MEMBER HAMMOND: I don't think --

14 PANEL MEMBER BLANC: But it's not so neatly --
15 it's not so neatly categorized, well, maybe that's how --

16 PANEL MEMBER HAMMOND: No, I think it does --

17 CHAIRPERSON FROINES: I think there are
18 differences of opinion about the strength of association.

19 PANEL MEMBER HAMMOND: No, I don't think it
20 changes the strength of association. But I think what it
21 does do is it reduces the probability that what you
22 observe is due to chance. And it does that by --

23 PANEL MEMBER BLANC: But that's not a
24 Bradford-Hill criterion.

25 PANEL MEMBER HAMMOND: Yes, it is. Yes, it is.

1 You want to --

2 CHAIRPERSON FROINES: Yes, it is. It's
3 consistency or --

4 PANEL MEMBER HAMMOND: No, it's different, but I
5 mean it's --

6 PANEL MEMBER GLANTZ: Yeah, that's true. I mean
7 in your -- worded the way you're wording it, it increases
8 your ability to estimate the level of consistency.

9 CHAIRPERSON FROINES: I mean one of the things
10 that we saw with diesel is we -- there are two or three
11 papers that took every epi-study and found fault with each
12 one; and at the end of it concluded, see, there's nothing
13 there. And so we know epidemiologists are very good at
14 slicing up an individual study.

15 But I think the going to the other extreme, where
16 you look at the meta-analysis and say it strengthens your
17 association, I'm not so sure one can do that either. But
18 I do think that it does indicate that the results may not
19 be results of chance or it adds to our success of
20 consistency. That's why everybody shows all these figures
21 with everything above the line, because you can see this
22 nice picture. And sometimes I think we have to be careful
23 about those kinds of pictures too. But in a sense the
24 meta-analysis does do that, don't you think?

25 PANEL MEMBER BLANC: And the other issue -- other

1 Bradford-Hill issue that we haven't talked about at all
2 today, and it's very absent from most of your arguments,
3 is the issue of specificity. And to me, that's a
4 demand -- how can you make that demand of something like
5 secondhand smoke that has, you know, 3,000 components to
6 it? Why should it have a specific effect, or why should a
7 health effect that it is associated with be specific only
8 to it when you would expect that other exposures would do
9 that?

10 PANEL MEMBER HAMMOND: That kind of goes back to
11 the microbial view of epidemiology, you know. And Sir
12 Richard Dole was actually talking about that on a campus
13 recently. Originally that was exactly the reason people
14 rejected the epidemiologic links between smoking and lung
15 cancer, is that as soon as they started having other
16 health effects related to smoking, then -- or other things
17 caused lung cancer, you know, so it couldn't be that
18 smoking was the cause. So it was -- and we know -- I
19 think that's something that we know better than now,
20 especially for complex mixtures. There are multiple
21 effects and there can be multiple causes.

22 PANEL MEMBER BLANC: Well, yeah, that was one
23 thing that Bradford-Hill developed, and he developed his
24 criteria in relationship to smoking and lung cancer. It
25 might be worth actually going back to the Surgeon

1 General's report and seeing how they spun that in that
2 context.

3 PANEL MEMBER GLANTZ: Oh, I don't know --

4 PANEL MEMBER BLANC: I would say, because if
5 you're going to -- you have invoked Bradford-Hill, you may
6 be invoking it more. If you're going to invoke it, you
7 better know what you're invoking. That's all I'm saying.

8 PANEL MEMBER GLANTZ: Well, why don't we go on
9 to Chapter 7.

10 CHAIRPERSON FROINES: Well, I think this --

11 PANEL MEMBER BLANC: I'm talking about the
12 respiratory, from my point of view.

13 CHAIRPERSON FROINES: Well, I think this is
14 useful, because in fact I think we're covering a lot of
15 ground I mean I thought we might end up covering come
16 January. So it's useful. And I think the broad outlines
17 are useful.

18 We're going to stop, I think what, Melanie?
19 2:15?

20 SUPERVISING TOXICOLOGIST MARTY: 2:15 to 2:30
21 would be good.

22 CHAIRPERSON FROINES: Yeah, because four of us
23 are on the same plane to Washington DC.

24 PANEL MEMBER GLANTZ: Now, is that a quorum?

25 That was a joke. That was a joke.

1 (Laughter.)

2 CHAIRPERSON FROINES: There are no jokes.

3 (Laughter.)

4 CHAIRPERSON FROINES: Go ahead, Melanie.

5 SUPERVISING TOXICOLOGIST MARTY: Okay. I think,
6 in view that we have a half an hour, we should not attempt
7 Chapter 7. It's a very large --

8 PANEL MEMBER BLANC: That's the cancer chapter?

9 SUPERVISING TOXICOLOGIST MARTY: That's the
10 cancer chapter.

11 PANEL MEMBER BLANC: I think you have to do the
12 breast cancer, skip right to -- in that chapter. You have
13 to do breast cancer. That's --

14 SUPERVISING TOXICOLOGIST MARTY: Do I have to do
15 breast cancer today?

16 PANEL MEMBER GLANTZ: Yes.

17 PANEL MEMBER BLANC: You have to do --

18 PANEL MEMBER BYUS: Yes, do it today. It's the
19 most controversial. We need the most time to think about
20 it.

21 SUPERVISING TOXICOLOGIST MARTY: Okay. Fine.

22 PANEL MEMBER HAMMOND: Get started --

23 PANEL MEMBER BYUS: Get start on it.

24 CHAIRPERSON FROINES: Yeah, because I think that
25 this will prepare -- everybody will realize they're going

1 to have go back and look very carefully at this issue
2 since it's so important.

3 That means for the panel, everybody is committed
4 to reading more and more and more over the Christmas
5 break.

6 CHAIRPERSON FROINES: Are you okay?

7 MR. MILLER: Yeah.

8 CHAIRPERSON FROINES: We have half an hour to go.

9 SUPERVISING TOXICOLOGIST MARTY: Okay. Mark
10 Miller is going to talk about the breast cancer section.

11 --o0o--

12 MR. MILLER: This is an overview of some of the
13 endpoints actually. It doesn't fit on a single slide with
14 the cancer chapter.

15 But the major changes --

16 CHAIRPERSON FROINES: Mark -- Peter, do you have
17 handouts?

18 MR. MATTHEWS: Yes.

19 MR. MILLER: Major changes since 1997. The lung
20 cancer argument was strengthened.

21 PANEL MEMBER GLANTZ: Just skip to breast cancer.

22 MR. MILLER: Okay. Breast cancer.

23 PANEL MEMBER GLANTZ: We speed through the rest
24 of those slides.

25 That was a joke.

1 MR. MILLER: So the studies of ETS and breast
2 cancer include case control studies, and most of which are
3 positive; and many are statistically significant so. Case
4 control studies with the best exposure assessment have the
5 highest risk estimates; many statistically significant.

6 There's several cohort studies. A few have
7 elevated but not significant findings. And some have null
8 results.

9 And the meta-analysis -- meta-analyses, both ours
10 and others, indicate elevated risk from ETS exposure.

11 --o0o--

12 MR. MILLER: And I thought we'd show two of the
13 studies we thought were among the strongest. One is the
14 relationship of breast cancer with passive and active
15 smoking, by Morabia. It's a population-based case-control
16 study with 244 cases and over a thousand controls.

17 And it was the first study to really do a good
18 job of the lifetime history of active and passive
19 exposure.

20 They went year by year from age 10 until the
21 interview. They created three separate calendars of
22 exposure for homework and leisure time. And in order
23 to -- passive smokers were defined as at least one hour a
24 day for at least 12 consecutive months.

25 The overall adjusted odds ratio for passive

1 exposure was 3.2, and that was significant.

2 So there was comparing passive smokers to a never
3 smoker/no environmental tobacco smoke exposure.

4 --o0o--

5 MR. MILLER: Similarly, the paper by Ken Johnson
6 from Health Canada looked at -- it was a registry
7 identified incident cases of breast cancer. There were
8 805 premenopausal breast cancers and 1512 post-menopausal.

9 There was a questionnaire with telephone
10 follow-up for each residence of at least a year. They
11 were questioned how many regular smokers were at that
12 residence for each job of a year or longer. They were
13 asked, "How many people regularly smoked in the subject's
14 immediate work area?"

15 --o0o--

16 MR. MILLER: And not only did they have positive
17 significant findings in the premenopausal breast cancer
18 area; they had a strong trend -- with P for trend --
19 .0007. This is for a total of residential and
20 occupational years exposed by years.

21 PANEL MEMBER BYUS: What does the "P for trend"
22 mean exactly? I mean what does that mean? It's in the --

23 MR. MILLER: I've had a statistician --

24 SUPERVISING TOXICOLOGIST MARTY: There's a trend
25 test that's done on dose response -- in this case, dose

1 response data. And it tells you whether there really is
2 an upward trend in that -- an upward dose response curve,
3 essentially, in this case. So it's --

4 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

5 SALMON: Essentially is the slope of the -- different from
6 one.

7 SUPERVISING TOXICOLOGIST MARTY: Right.

8 CHAIRPERSON FROINES: Does he mention the healthy
9 worker survivor effect in this paper?

10 SUPERVISING TOXICOLOGIST MARTY: I don't think he
11 relates the -- I don't think he does discuss the healthy
12 worker effect. But this occupational plus residential
13 exposure.

14 --o0o--

15 MR. MILLER: Looking at the cohort studies, there
16 were two that had elevated risk, Hirayama and Jee. And an
17 additional four that were not elevated. Neither of the
18 two that were elevated were statistically so. Although
19 they both -- the two that looked at premenopausal risk had
20 elevations, neither of which was statistically either.

21 PANEL MEMBER BLANC: You say cohort. You mean
22 longitudinal? You tend to use the word "cohort" as if you
23 meant longitudinal.

24 MR. MILLER: Prospective cohort study. Yeah, it
25 was --

1 PANEL MEMBER BLANC: But both the cross-sectional
2 ones were cohort studies too. They were cross-sectional
3 cohort studies, weren't they?

4 MR. MILLER: Yeah.

5 PANEL MEMBER BLANC: So I would suggest it would
6 be cleaner, when you mean longitudinal, just say
7 longitudinal; when you mean cross-sectional, say
8 cross-sectional.

9 MR. MILLER: Okay.

10 --o0o--

11 MR. MILLER: I'd like to address head-on the
12 results of cohort versus case control studies.

13 Some of the non-U.S. studies showed elevated
14 non-significant risks. We just mentioned that.

15 To date, none of the cohort studies have measures
16 of exposures that include childhood, residential adult,
17 and occupational information of exposure.

18 SUPERVISING TOXICOLOGIST MARTY: Mark, let me
19 interject here.

20 The reason we're discussing this is because a lot
21 of people have said, "Well, those cohort studies weren't
22 positive. And prospective cohort studies are the gold
23 standard of epidemiology." So, therefore, in their minds
24 they don't believe the case control.

25 PANEL MEMBER HAMMOND: Hence, Paul's point, so

1 important --

2 SUPERVISING TOXICOLOGIST MARTY: Right.

3 PANEL MEMBER HAMMOND: -- that these aren't
4 cohort studies. They aren't gold standards.

5 SUPERVISING TOXICOLOGIST MARTY: Right.

6 MR. MILLER: You know -- well, we'll get to it.

7 As an example though, we'd like to point to
8 Fontham, which was a case-control study and is readily
9 recognized as the best lung cancer study because it had
10 the best exposure history and it included all the relevant
11 exposures and cotinine measurements. And it was a large
12 study with a variety -- you know, a large varied
13 population.

14 The bottom line is that we feel that the cohort
15 study is only as good as exposure assessment.

16 PANEL MEMBER BLANC: Could we go back -- go back
17 to the cohorts again.

18 How long was the follow-up in these cohort
19 studies?

20 MR. MILLER: Oh, they varied.

21 SUPERVISING TOXICOLOGIST MARTY: They varied.

22 MR. MILLER: From a few years to 16 years,
23 something like that.

24 PANEL MEMBER BLANC: And they were prospective
25 cohort studies, all of them?

1 MR. MILLER: Prospective cohort --

2 SUPERVISING TOXICOLOGIST MARTY: Those were.

3 PANEL MEMBER BLANC: Cohort studies.

4 And the only measure of ETS exposure was the ETS
5 exposure at the initiation of the cohort?

6 MR. MILLER: Well, they vary. But often that's
7 the case, is a single -- I mean, for example, Wartenburg
8 had -- well, the primary information was from the
9 husband's questionnaire, so there was some information
10 there. And then from the woman's questionnaire, it was
11 "What is your exposure" -- "Does your husband smoke now,
12 in 1983?" So that it didn't include historical
13 information and didn't reassess it over the 16 years or so
14 that --

15 PANEL MEMBER BLANC: Uh-huh.

16 MR. MILLER: So they vary from study to study.
17 But they often are a single time point, they often are,
18 you know, only spousal information.

19 PANEL MEMBER BLANC: Are these studies able to
20 show an association between direct smoking and breast
21 cancer?

22 MR. MILLER: Reynolds is one to point to, which
23 is a recent study in California. It was --

24 SUPERVISING TOXICOLOGIST MARTY: I think there
25 was only one.

1 Well, no, that's not the only one. Wartenburg,
2 the active smoking part of that was called Calle
3 C-a-l-l-e, which was published many years prior to
4 Wartenburg. And they found an association with active
5 smoking.

6 Egan finds an association -- you have to -- if
7 you look at women who started smoking 16 years or younger,
8 there was a statistically significant positive association
9 in Egan.

10 Reynolds had an overall association, even though
11 the only measure of exposure was residential exposure from
12 Reynolds.

13 PANEL MEMBER BLANC: The reason I asked the
14 question is because if their risk estimates of direct
15 smoking associated with the breast cancer were
16 substantially diluted compared to other people's risk
17 estimates of direct smoking and cancer, that might support
18 your argument that the -- and assuming that it had the
19 sort of the same tendencies of not having good interval
20 information and so forth, it would perhaps support your
21 argument that there was too much exposure
22 misclassification to give that it diluted it towards the
23 null.

24 Am I making sense?

25 AIR TOXICOLOGY AND RISK ASSESSMENT UNIT CHIEF

1 SALMON: The big concern with the proposal that the ETS is
2 associated with breast cancer has been the fact that the
3 association with active smoking is being regarded dubious
4 at best precisely because these studies -- apart from
5 Reynolds, which is a much more recent study, the previous
6 studies generally have had a very diluted and dubious
7 association with active smoking.

8 SUPERVISING TOXICOLOGIST MARTY: We're going to
9 get into that. We should just keep going on this
10 presentation.

11 PANEL MEMBER GLANTZ: I think it would be good to
12 let them go through this, and then come back to the
13 questions.

14 MR. MILLER: There's a Whole convergence of
15 different information.

16 PANEL MEMBER BLANC: Okay. Go to your next one.

17 --o0o--

18 MR. MILLER: So to start with -- and then we'll
19 move backwards -- we did this meta-analysis with Ken
20 Johnson from Health Canada and looked at 17 studies, of
21 which five assessed childhood, adult residential,
22 occupational and social exposures.

23 --o0o--

24 MR. MILLER: Overall the 17 studies were a
25 heterogeneous group. But if you looked at the studies

1 that collected the important sources of exposure, there
2 was a homogeneous group. And our results were consistent
3 with previous meta-analyses by Wells, Morabia, Khuder and
4 Simon.

5 --o0o--

6 MR. MILLER: So here's -- just to look at those
7 studies, the ones with the black triangles are
8 statistically significant results.

9 The summary estimate for all studies was -- 1.31
10 was statistically significant. And if you isolated the
11 studies with the more complete exposure assessment, that
12 increases to 1.89.

13 Next slide.

14 --o0o--

15 MR. MILLER: Similarly -- this is looking at the
16 studies that isolated premenopausal breast cancer. And as
17 you see, all of the results were positive, and many of the
18 studies were significantly so. And also again a slight
19 increase in the risk estimates when you look at just the
20 studies that had more complete exposure assessment.

21 --o0o--

22 MR. MILLER: So --

23 CHAIRPERSON FROINES: Sorry. Go back to that --
24 Just one second.

25 MR. MILLER: This is premenopausal risk.

1 CHAIRPERSON FROINES: Hirayama is where?

2 MR. MILLER: Hirayama's at the beginning here,
3 '84.

4 CHAIRPERSON FROINES: And Wartenburg -- am I
5 misreading it? -- it also doesn't show a significant
6 result.

7 SUPERVISING TOXICOLOGIST MARTY: Right.

8 CHAIRPERSON FROINES: Right.

9 CHAIRPERSON FROINES: Go ahead.

10 PANEL MEMBER BLANC: And you're saying that Egan,
11 for example, doesn't differentiate between pre
12 postmenopausal breast cancer?

13 MR. MILLER: Right. It was all premenopausal for
14 Egan.

15 And Shrubsole -- you know, I mean we chose this,
16 which was an overall number. However, if their estimate
17 for work exposure was actually 1.6, then was statistically
18 significant.

19 --o0o--

20 MR. MILLER: Historically, essentially what was
21 said in the 1997 document was, well, we have these several
22 studies that look at passive smoking. And all of them
23 look suggestive or positive. But when we look at the
24 cohort studies, we're not so sure. Actually when they
25 look at the active study -- active smoking studies, it's

1 more of a mixed bag. And so that we don't know how to
2 interpret this.

3 So the effect, seeing active smokers were
4 comparable or weaker to those seen in passive smoking,
5 they were also concerned that there were no dose response
6 trends that were evident in the data and that there was
7 uncertainty about the suggestion that there were certain
8 susceptible subgroupings of women.

9 --o0o--

10 MR. MILLER: So there are various hypotheses that
11 may help to explain some of those findings, and we've
12 started talking about those already. But there's a
13 causal -- or presumed to be a causal preventive effect
14 from current active smoking, and that's
15 anti-estrogenicity. It may obscure an overall association
16 between smoking and breast cancer.

17 While there's some variation in studies that have
18 looked at the actual estrogen levels, there is an increase
19 in the less active estradiol and relative to the more
20 active 16-hydroxy estradiol.

21 There's also in numerous studies estrogen effect
22 that's noted: Decrease in age at menopause, which is an
23 anti-estrogen effect; increase in breast density;
24 attenuated effects of hormone replacement; and increased
25 risk of osteoporosis.

1 So the risk was similar for active and passive
2 exposure. This is another hypotheses. And that
3 highlights a need for unexposed controls.

4 Next.

5 --o0o--

6 MR. MILLER: That sensitive subpopulations or
7 time periods exist. For example, polymorphisms in
8 metabolism. There's windows of susceptibility, either
9 peri--pubertal or before the first pregnancy. And that
10 there's a need to examine long durations of exposures, 30
11 to 40 years. And particularly in the earlier studies it
12 was difficult to find women that would fit into that
13 category.

14 Next slide.

15 --o0o--

16 MR. MILLER: In examining windows of
17 susceptibility, one important part of the argument is the
18 breast biology. There's several periods of breast
19 epithelial development. Lobules go through cell division
20 and differentiation. They're quite immature up until
21 peripuberty when they develop lobules. Then those further
22 differentiate during pregnancy and lactation.

23 --o0o--

24 MR. MILLER: In vitro studies there's some
25 support for this. The lobules of varied differentiation

1 were isolated from reduction mammoplasty and cultured.
2 And the least differentiated cells from the nulliparous
3 women were most susceptible to transformation by Benzoate
4 Pyrene and nitrosamines than the more differentiated cells
5 from women that have had pregnancies. This is similar to
6 findings in rodent cells.

7 --o0o--

8 MR. MILLER: As well, there's a series of studies
9 that was reviewed by Russo and Russo, where PAH induced
10 mammary tumors in the rat model revealed the period of
11 greatest mammary differentiation was the most susceptible
12 period and that reduced sensitivity of mammary epithelium
13 was seen after pregnancy and lactation, which could be
14 mimicked by injection with chorionic gonadotrophin.

15 --o0o--

16 MR. MILLER: As well in human studies from
17 radiation exposure, we know that there's significant
18 increase in breast cancer. For example, in women -- in
19 girls that were treated with radiations of the chest for
20 Hodgkins lymphoma, in fact that's 75 times the background
21 incidence. But if you look at the ones that were treated
22 between 10 and 16 years of age and compare those to the
23 ones that were treated under 10 years of age, there's over
24 a six-fold increase in those treated during adolescence.
25 And that's consistent with other studies, both bomb

1 survivors and radiation from x-rays for girls that have
2 had scoliosis and rods placed in their back.

3 --o0o--

4 MR. MILLER: So looking at these factors, in kind
5 of an interesting and complex study, Band did a study of
6 active smoking; looked at the odds ratios relative to
7 non-smokers; and explored these hypotheses of interaction
8 between active smoking's anti-estrogenic effects, which
9 are protective, and windows of susceptibility to the
10 carcinogenic effects.

11 --o0o--

12 MR. MILLER: And one part of the hypothesis would
13 be the tumorigenic action of the carcinogens would be
14 displayed most prominently with exposure prior to first
15 pregnancy and during peripubertal times. The idea is that
16 the breast sensitivity at that point would outweigh any
17 anti-estrogenicity. So in order to look at that, they
18 looked at premenopausal breast cancer by the timing of the
19 initiation of smoking so that those that initiated earlier
20 in life, less than five years after menarche, had a
21 significantly more elevated risk, OR 1.7, compared to
22 those that started more than five years after, or also
23 looking at it similarly in relation to the first
24 pregnancy.

25 If you initiated smoking before your first

1 pregnancy, you had increased risk. Whereas if you
2 initiated after your first pregnancy, you did not.

3 And the extreme example is that a nulliparous
4 woman and with a high exposure, she would have an odds
5 ratio over seven-fold.

6 --o0o--

7 MR. MILLER: So the other side of the argument is
8 that anti-estrogenicity as a protective effect would be
9 most pronounced in postmenopausal women, with onset of
10 smoking after the first pregnancy and relatively heavy.
11 That relates to the estrogen levels being higher in those
12 postmenopausal women due to aromatization of adrenal
13 androgens and that they would have avoided the exposure in
14 the earlier sensitive period.

15 And, indeed, what seen in those women, that those
16 who initiated smoking after the first pregnancy and gained
17 weight had an odds ratio of .49, which was statistically
18 significant; and those who initiated after the first
19 pregnancy did not have a significant.

20 --o0o--

21 MR. MILLER: So in regards to the risk being
22 similar for active and passive exposure, here's several
23 recent studies that would be considered as good exposure
24 assessment studies that do have active and passive odds
25 ratios that are similar.

1 PANEL MEMBER GLANTZ: So were those -- if you go
2 back. The ones that are active smoking studies, were
3 those ones where they were using as the control group,
4 non-exposed nonsmokers?

5 MR. MILLER: Yeah, I think --

6 PANEL MEMBER GLANTZ: Or was that all nonsmokers?

7 MR. MILLER: Non-exposed nonsmokers. I think
8 Lash was actually a variation on that, but more or less.

9 PANEL MEMBER GLANTZ: Okay.

10 --o0o--

11 MR. MILLER: So there's a similar dose response
12 for active and passive smoking, maybe related to differing
13 chemical composition of mainstream and ETS. There are
14 more carcinogens in the latter.

15 Dose response is difficult to characterize. And
16 that's maybe because it's a non-linear for breast cancer.
17 It's complicated by anti-estrogenic activity of active
18 smoking, genetic polymorphisms and windows of
19 susceptibility, as we've been talking about.

20 --o0o--

21 MR. MILLER: This is from Morabia, looking at
22 active smoking, and highlights that -- you know, this is
23 adjusted smokers versus nonsmokers with no ETS, with
24 elevated odds ratios. For example, 10 to 19 cigarettes
25 per day, 2.7.

1 And then if you look at that -- instead of
2 comparing it to smokers to nonsmokers without ETS, you
3 just compare smokers to nonsmokers, which includes ETS
4 exposed. You can see that each of the odds ratios drops
5 significantly. And in fact, you know, for the lower
6 exposure groups it goes from an elevated pretty much
7 significant value to a non-significant value.

8 Similar results within individual studies are
9 found in Johnson, Lash and Aschengrau, and Kropp and
10 Chang. So this has been validated in a number of
11 different studies.

12 --o0o--

13 MR. MILLER: On top of that, looking at even --
14 considering that, looking at the active smoking studies
15 and breast cancer, there's still considerable evidence
16 that active smoking does appear to be related to breast
17 cancer.

18 --o0o--

19 MR. MILLER: Do you want to do this?

20 SUPERVISING TOXICOLOGIST MARTY: Yeah. Mark's
21 having throat difficulty.

22 Just wrap this up.

23 CHAIRPERSON FROINES: Why don't we -- we're at a
24 place that's a good place to stop I think, unless you want
25 to --

1 PANEL MEMBER GLANTZ: If we could, I think it
2 would be nice to just hear the whole thing and the --

3 CHAIRPERSON FROINES: We can't, Stan. We have
4 four people making a plane to Washington. We can't --

5 PANEL MEMBER GLANTZ: Oh. I thought you said we
6 could go till 2:30. No?

7 CHAIRPERSON FROINES: No.

8 SUPERVISING TOXICOLOGIST MARTY: I could move
9 through a few more slides really quickly and finish.

10 PANEL MEMBER GLANTZ: Okay.

11 SUPERVISING TOXICOLOGIST MARTY: Would that be
12 okay?

13 CHAIRPERSON FROINES: Well, my only concern is
14 you're getting into an area that I have rather strong
15 feelings about the science. And so when we get into
16 mammary carcinogens and PAH and tobacco smoke and those
17 things, if you want to skip those and come back to them
18 next time, because there's going to be discussion I think
19 associated with that.

20 I hate to sort of say -- I mean then I would skip
21 to someplace where -- why don't you skip to "Comments" if
22 you're going to --

23 PANEL MEMBER HAMMOND: We'll have discussions on
24 them in January. I just thought this was just to --

25 CHAIRPERSON FROINES: Then why can't -- I would

1 like to be leave for the airport right this minute. And
2 Stan wants us to go in 15 minutes so we can get --

3 PANEL MEMBER BLANC: Who are the two leads on
4 this? Stan -- on cancer, the two of you?

5 What I would suggest is -- we have the copy of
6 the slides handed out -- that we adjourn essentially now.
7 People can look at the slides.

8 But I would also appreciate at some point between
9 now and the January meeting in advance of the January
10 meeting to have some brief comments from the leads on this
11 chapter, not on the whole chapter, but on the breast
12 cancer piece of it, because I perceive that this is going
13 to be one of the more contentious and perhaps -- could
14 perhaps lead to avoidable delays in the document. If
15 there's some parts of it that we can thrash out or lay out
16 the issues more clearly in advance of the January meeting.

17 PANEL MEMBER GLANTZ: Well, do you think -- I
18 mean is there any chance even if John left that we could
19 just continue talking?

20 PANEL MEMBER BLANC: No. He said four people on
21 the plane.

22 CHAIRPERSON FROINES: I'm the Chair, and I'm not
23 leaving --

24 PANEL MEMBER GLANTZ: Well, do you want to just
25 say just on the record what your concerns are just so we

1 know what they are?

2 CHAIRPERSON FROINES: No, I don't think -- Stan,
3 I think that what you're doing is you're trying to hurry a
4 process that doesn't -- that won't get better by hurrying
5 it.

6 PANEL MEMBER GLANTZ: Well, I'm not trying to
7 hurry it. I'm just trying to understand.

8 CHAIRPERSON FROINES: Well, I don't think we
9 should get into -- I don't think we should get into
10 substance because that's going to get us into a lengthy
11 discussion.

12 PANEL MEMBER GLANTZ: Okay.

13 CHAIRPERSON FROINES: And I think that -- I don't
14 think -- let me be very clear.

15 This process is not going to be hurried. No
16 matter how much you want this to go through, it's not
17 going to be hurried, because I want the record to indicate
18 a very thorough careful analysis of all the data. And we
19 have to do that. And so it's sort of like saying, "Can't
20 we just hear what your concerns are and spend ten more
21 minutes?" It's exactly the opposite of what I think we
22 should be doing.

23 PANEL MEMBER GLANTZ: No -- and I'm not -- I mean
24 I'm not disagreeing with you. I think we want to be
25 careful. But I would have liked to have just heard the

1 rest of the presentation, because it gives us something to
2 think about.

3 But if you don't want to do that, we can stop.

4 CHAIRPERSON FROINES: No. Let me just make
5 clear.

6 We are going to hear the presentation. We're
7 just going to hear it at the next meeting.

8 PANEL MEMBER BYUS: I have a brief request along
9 the line of what you're saying. Why don't we try and
10 prepare some written questions and written comments that
11 can help you guide the next meeting in terms of
12 constructing an agenda for it in terms of focusing on some
13 issues. That's what I think you were getting at.

14 CHAIRPERSON FROINES: Well, I think that's fine.
15 I think the important thing is to follow the process that
16 we've established; namely, that if Paul has questions, he
17 communicates that to the leads, and the leads communicate
18 it to the OEHHA, so we keep an orderly kind of structure.

19 PANEL MEMBER GLANTZ: Well, I think that's fine.

20 CHAIRPERSON FROINES: And so that means people
21 who have questions communicate with Joe and Stan. Who
22 else was doing cancer?

23 PANEL MEMBER GLANTZ: Well, my only concern
24 here -- I'm fine with that. But what I would like to
25 see -- because, frankly -- I mean I've looked through the

1 drafts of the documents and raised the issues that I
2 raised, which have been addressed. So I think I would
3 personally -- if John or other people have issues that
4 they think ought to be addressed, I would rather do what
5 John just said, and we can transmit that to the staff to
6 try to get them addressed before the next meeting.
7 Because I don't think -- I don't think I have much to say,
8 frankly, that would be of much value. I'm much more
9 interested in hearing what the other people here have to
10 say. So I would suggest we do that.

11 And can I just ask one other question?

12 And that leaving aside this discussion, there
13 have been a whole bunch of suggestions made about parts of
14 the report that have been discussed up to this point, and
15 there have been a bunch of sort of generic suggestions
16 made about the introductions and the tables and things
17 like that. Would it be sensible or a good use of time to
18 ask OEHHA to do a red-line and strike-out revision of the
19 document based on the discussion so far before the next
20 meeting, or is that a waste of time?

21 CHAIRPERSON FROINES: Melanie.

22 (Laughter.)

23 SUPERVISING TOXICOLOGIST MARTY: Well, we could
24 do the easy stuff. But I'm not sure how useful that would
25 be since most people have already written comments in the

1 margin of the copy they have.

2 It might be -- I think a better idea is to make
3 sure that the transcript gets back to the panel members so
4 they know what's already been asked of us. I think that
5 might be helpful.

6 PANEL MEMBER GLANTZ: Well, do you see any of the
7 things that were raised as substantive, or you see them as
8 primarily editorial in nature?

9 SUPERVISING TOXICOLOGIST MARTY: Is this is a
10 trick question?

11 PANEL MEMBER GLANTZ: No.

12 (Laughter.)

13 SUPERVISING TOXICOLOGIST MARTY: No, there were
14 substantive issues raised. I mean one of the things is
15 the preterm delivery. Are we going to call that causal or
16 not? I mean that's a --

17 PANEL MEMBER GLANTZ: Okay. Well, I would hope
18 then for the next meeting that of the stuff -- that you
19 guys look through the transcript, and of the issues that
20 were raised that you think are substantive, that when you
21 come back next time that you have sort of what your
22 response to the panel is on those points. You know, you
23 don't necessarily have to revise the document. But so
24 that there can be -- you know, so you guys can come back
25 and say, "Okay, you guys brought these issues up. Here's

1 what we're recommending saying:" So that there'll be some
2 closure to those questions.

3 And, again, I would just ask if -- I would
4 personally -- I mean personally if people have issues with
5 this stuff -- and I agree with you that the breast cancer
6 stuff is very important and we don't want to rush it. But
7 it would be helpful I think if those issues could be
8 brought to OEHHA's attention so they can come to the
9 meeting next time prepared to address them rather than
10 hearing them called.

11 CHAIRPERSON FROINES: Joe.

12 PANEL MEMBER LANDOLPH: You want us to give
13 written comments to you to give to OEHHA? Or what do you
14 want to do?

15 CHAIRPERSON FROINES: I thought it would be
16 easier if any comments went to the leads, who then had
17 responsibility for making sure there was communication
18 rather than a sort of individual process that is kind of
19 just more disorganized.

20 PANEL MEMBER GLANTZ: Okay. I mean I think
21 that's fine.

22 PANEL MEMBER LANDOLPH: Send us stuff to take --

23 CHAIRPERSON FROINES: What I would do is copy
24 Melanie on what you send to Stan. And so in case there's
25 a glitch, that both people have them.

1 But -- I, for example, have some questions about
2 the Part A document. And I didn't raise them because of
3 the timing situation. I think Kathy does too.

4 So there are lots -- there are still unresolved
5 issues. And I think just -- not to sound overbearing at
6 all, because I don't mean to be -- but I think this
7 process is going to go -- it's going to take awhile, and
8 we're going to have to do it very systematically. And
9 so -- that doesn't mean we have to go, you know,
10 glacially --

11 PANEL MEMBER BLANC: I'm going to make a motion
12 that we adjourn.

13 PANEL MEMBER LANDOLPH: Second.

14 PANEL MEMBER BYUS: Third.

15 (Laughter.)

16 CHAIRPERSON FROINES: All in favor?

17 (Hands raised.)

18 (Thereupon the California Air Resources Board,
19 Scientific Review Panel meeting adjourned
20 at 2:20 p.m.)

21

22

23

24

25

1 CERTIFICATE OF REPORTER

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

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

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

14 IN WITNESS WHEREOF, I have hereunto set my hand
15 this 6th day of December, 2004.

16

17

18

19

20

21

22

23

JAMES F. PETERS, CSR, RPR

24

Certified Shorthand Reporter

25

License No. 10063