

MEETING  
STATE OF CALIFORNIA  
AIR RESOURCES BOARD  
SCIENTIFIC REVIEW PANEL

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1 PROCEEDINGS

2 CHAIRPERSON FROINES: I'd like to call the  
3 meeting to order.

4 We now have everybody here who's going to be  
5 here. We will be missing one panel member, Dr. Charles  
6 Plopper from UC Davis, who's traveling in Sweden.

7 And so at this point I'll open the meeting of the  
8 Scientific Review Panel on September 26th, 2007. And we  
9 have a quorum.

10 And so we should just begin with ethylbenzene.  
11 And, Andy, it looks like you're on target.

12 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

13 CHIEF SALMON: Yes. Well, we're going to get  
14 euphemistically -- we're going to get closer to the  
15 microphone first.

16 We're going to start with a brief presentation on  
17 our derivation of the unit risk factor for ethylbenzene,  
18 which is going to be given by Dr. Joe Brown here.

19 So I'll hand it straight over to you, Joe.

20 OEHHA STAFF TOXICOLOGIST BROWN: Thank you, Andy.

21 CHAIRPERSON FROINES: Excuse me. Paul wanted to  
22 ask a question.

23 PANEL MEMBER BLANC: Well, I was just going to  
24 say, Andy, you should give your full name, because  
25 otherwise on the transcript people may think your name is

1 Ethyl Benzene.

2 (Laughter.)

3 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

4 CHIEF SALMON: Well, I've been called a -- I've  
5 been called a number of names in my time, but that is an  
6 innovation.

7 For the record, my name is Dr. Andrew G. Salmon,  
8 and I'm Chief of the Air Toxicology and Risk Assessment  
9 Section of OEHHA.

10 CHAIRPERSON FROINES: And you might -- one of you  
11 might just make sure that we all understand why this  
12 chemical is coming forward at this particular time.

13 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

14 CHIEF SALMON: Okay. Well, I think Joe will  
15 probably cover that. But in a nutshell, this is a  
16 chemical which is identified as a hazardous air pollutant  
17 by the federal forces; and, therefore, by definition is  
18 also a toxic air contaminant. It's a compound which is  
19 somewhat ubiquitous in the environment and from a various  
20 sources, as you will hear. And as a result of recent  
21 work, there are some carcinogenicity findings, which give  
22 us cause for concern. So this is what prompted us to  
23 derive a unit risk factor to assist the -- particularly  
24 the Air Toxics Hot Spots Program in any situations where  
25 they would want to warn or regulate a chemical.

1 CHAIRPERSON FROINES: Is there monitoring that's  
2 been occurring for ethylbenzene?

3 OEHHA STAFF TOXICOLOGIST BROWN: Yes, I believe  
4 so.

5 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

6 CHIEF SALMON: Yes, they -- I mean that is  
7 something, you know, for the details we should defer to  
8 the Air Resources Board staff. But in a word, yes.

9 (Thereupon an overhead presentation was  
10 Presented as follows.)

11 OEHHA STAFF TOXICOLOGIST BROWN: Thank you, Andy.

12 Let's get the next slide here, take a look at  
13 ethylbenzene.

14 --o0o--

15 OEHHA STAFF TOXICOLOGIST BROWN: As you can see,  
16 similarities to benzene and styrene, two other compounds  
17 we're familiar with, were studied. And it is a federal  
18 HAP under the U.S. Clean Air Act, 1990, and therefore it's  
19 a toxic air contaminant.

20 Next slide.

21 --o0o--

22 OEHHA STAFF TOXICOLOGIST BROWN: As Andy  
23 mentioned, many sources:

24 Industrial emissions, over 7 million pounds in  
25 2002. Hopefully that's gone down.

1 Vehicle exhaust.

2 Wood burning.

3 It's a component of environmental tobacco smoke.

4 And we have a 2005 figure for ambient air  
5 concentration in California of .22 parts per billion or  
6 .96 micrograms per cubic meter.

7 Next.

8 --o0o--

9 OEHHA STAFF TOXICOLOGIST BROWN: Just for  
10 reference, you know, established a chronic REL in 2000 of  
11 2,000 grams per cubic meter, or 400 ppb, based on  
12 nephrotoxicity, hyperplasia of the pituitary gland, and  
13 other affects.

14 Next slide.

15 --o0o--

16 OEHHA STAFF TOXICOLOGIST BROWN: Carcinogenicity.  
17 The gene tox profile for this we feel at this point is  
18 sort of inconclusive. However, the NTP in 1999 ran a full  
19 bioassay on this in mice and rats. They found:

20 Clear evidence of renal tubular adenoma or  
21 carcinoma and testicular adenoma in male rats;

22 Some evidence of renal tubular adenoma in female  
23 rats; and

24 Clear evidence for both lung and liver tumors in  
25 male and female mice, respectively.

1 Next.

2 --o0o--

3 OEHHA STAFF TOXICOLOGIST BROWN: This gives a  
4 rundown of the actual quantal responses for the five tumor  
5 sites that were identified, from top to bottom mice to  
6 rats.

7 And in the first column there you can see that  
8 all of the tests gave significant trends for increases in  
9 the tumor incidents with dose. And also the top doses  
10 were all significantly different by the Fisher exact test.

11 And the denominators on these quantal responses  
12 ignored any animals that died before the first particular  
13 tumor was observed. So these are sort of adjusted by  
14 this.

15 Next slide, please.

16 --o0o--

17 OEHHA STAFF TOXICOLOGIST BROWN: Okay. In terms  
18 of dose response methods, we actually apply two.

19 We use the sort of traditional approach,  
20 linearized multistage model, using the MSTAGE program of  
21 Couch, 1992.

22 And we also use the benchmark dose methodology  
23 first introduced by U.S. EPA in 1996, and using the EPA  
24 software. The latest version of this actually just came  
25 out last week. It's version 1.4.1B. But they keep

1 updating this as we go forward inside.

2           Now, we also use two different dose metrics. We  
3 use sort of an applied dose or a lifetime weighted average  
4 daily dose. And we also used a pharmacokinetic model to  
5 produce sort of a PBPK adjusted dose. And in  
6 extrapolating from the animal data to the human potency  
7 values or unit risks, we apply two different factors. For  
8 the applied dose, we used body weight human over body  
9 weight animal to the one-fourth power. And for the  
10 pharmacokinetic metric we used a smaller factor because we  
11 assumed the model would take part of that adjustment --  
12 would take care of part of that adjustment. So we used a  
13 one-eighth power adjustment in this case.

14           PANEL MEMBER GLANTZ: That was one thing in  
15 reading the report I -- was that just --

16           MR. MATHEWS: Into the mic.

17           PANEL MEMBER GLANTZ: Oh, I'm sorry.

18           I didn't -- I mean what was -- other than just  
19 seeing what you just said that it seemed like less of an  
20 adjustment made sense. Is there any literature --

21           OEHHA STAFF TOXICOLOGIST BROWN: Yeah, there was  
22 a rationale for that. The interspecies scale really is  
23 considered to be two components, pharmacokinetic component  
24 and a pharmacodynamic component. And, you know, it's an  
25 argument -- I guess we could argue how we should parcel

1 these two. We sort of assumed sort of arbitrarily that  
2 they're equal -- that they make equal contributions. Now,  
3 maybe that's not exactly true. But in this case, I think  
4 it's just an assumption of the assessment that we're doing  
5 here. That may not always be exactly the case. But in  
6 this case we're assuming that half of that interspecies  
7 correction is due to pharmacokinetics, which we're  
8 accounting for in the modeling. So this is more or less  
9 an assumption than assessment.

10 PANEL MEMBER GLANTZ: So it's just an assumption  
11 you made?

12 OEHHA STAFF TOXICOLOGIST BROWN: Yeah.

13 PANEL MEMBER GLANTZ: There's no data to --

14 OEHHA STAFF TOXICOLOGIST BROWN: It might not be  
15 half-half. It might be two-thirds and one-third.

16 Andy, do you want to say a word?

17 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

18 CHIEF SALMON: As an aside, I'll just remark that  
19 the one-quarter power effect, which was the default for  
20 the applied dose method, is the recommended default for  
21 the new U.S. EPA 2006 cancer risk assessment guidelines.  
22 And it's what we are generally proposing to use ourselves  
23 for risk assessment at this point. So that is the  
24 underlying policy default.

25 PANEL MEMBER GLANTZ: Well, I think -- I mean I

1 think it would be helpful in the report to just make this  
2 clear, because when I read it I couldn't quite figure -- I  
3 mean I sort of generally remember that one-quarter number  
4 from somewhere a long time ago. But I think being  
5 explicit about where you got those from and what  
6 assumption you're making, I think would just make the  
7 report clearer, as I was very confused by that.

8 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

9 CHIEF SALMON: We'll clarify that.

10 OEHHA STAFF TOXICOLOGIST BROWN: So actually to  
11 recap here --

12 CHAIRPERSON FROINES: Let me just ask a question.

13 The difficulty I have, being the chemist in the  
14 crowd, is you say pharmacokinetic and pharmacodynamic, and  
15 I don't have anything to connect that to. I don't have  
16 any chemistry to connect what in fact you are talking  
17 about.

18 OEHHA STAFF TOXICOLOGIST BROWN: Okay. Let me  
19 try to explain that a little bit better.

20 The pharmacokinetics, you can view this as  
21 basically what the body does to the chemical. And the  
22 pharmacodynamics is -- you know, is the other way around.  
23 So it's the biological response as opposed to the  
24 metabolism and the distribution.

25 So pharmacodynamics is a response -- a biological

1 response to the chemical, what the chemical is doing to  
2 the body rather than what the body is doing to the  
3 chemical.

4 CHAIRPERSON FROINES: I think everybody at the  
5 table knew that. That's why we're here.

6 PANEL MEMBER BLANC: Oh, I thought that was a  
7 nice summary, to tell you the truth. I mean it was a nice  
8 way of saying it.

9 OEHHA STAFF TOXICOLOGIST BROWN: But that's the  
10 simplest way I can explain it.

11 So pharmacokinetics deals with uptake  
12 distribution and metabolism, but it doesn't deal with  
13 response per se or particular --

14 CHAIRPERSON FROINES: Well, let me give you -- I  
15 don't want to prolong this, but let me give you an  
16 example. When we did the pharmacokinetic modeling for  
17 methylene chloride, we were concerned about the  
18 glutathione pathway and the P-450 pathway. And here we  
19 have evidence for the formation of a hydroquinone as a  
20 metabolic pathway.

21 And so when you're talking about -- when you give  
22 the basic definition of toxicokinetics, the question is:  
23 What are the elements that went into developing the models  
24 besides in terms of your thinking? I mean I  
25 understand -- I understand that these are approaches that

1 one can take without taking into consideration the actual  
2 what does pharmacodynamics mean within this context.

3 OEHHA STAFF TOXICOLOGIST BROWN: Well I think it  
4 means the -- you know, the anticipated human response to  
5 this chemical, which we don't know for sure. So we're  
6 trying to adjust for, you know, how it might be  
7 metabolized and excreted. But we don't know -- we're not  
8 too sure about the response side of it, you know, what is  
9 happening in at a tissue level.

10 CHAIRPERSON FROINES: Okay. We'll just leave it  
11 as it is.

12 PANEL MEMBER FRIEDMAN: So I just want to make  
13 sure I understand it.

14 So you're saying that, you know, if you just took  
15 the human weight divided by the animal weight, a human so  
16 much bigger than a rat or a mouse, that you'd have a huge  
17 difference in effect; but you're saying that it probably  
18 has more -- we're assuming that it has more of an effect  
19 on the human than the rate difference -- than the weight  
20 difference would imply?

21 OEHHA STAFF TOXICOLOGIST BROWN: Yes.

22 PANEL MEMBER FRIEDMAN: Is this just sort of a  
23 safety consideration or is this based on actual knowledge  
24 of the effects on humans versus animals?

25 OEHHA STAFF TOXICOLOGIST BROWN: Well, you know,

1 there are studies studying various scaling factors, mainly  
2 in sort of anti-cancer drugs and things like this. But  
3 when you get down to the environmental chemicals, it's a  
4 little bit more difficult to predict how the body's going  
5 to respond.

6 PANEL MEMBER FRIEDMAN: I didn't understand what  
7 you said.

8 OEHHA STAFF TOXICOLOGIST BROWN: When you get  
9 down to environmental chemicals like this, the not  
10 anti-cancer drugs that have been studied in humans.

11 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

12 CHIEF SALMON: You know, there's a -- there have  
13 been a number of studies of the relative potency of  
14 carcinogens in animals of different sizes including  
15 humans. And as Joe says, the data set is defective in the  
16 sense that most of the ones obviously are drugs. But,  
17 nevertheless, there are actually quite a number of data  
18 points now. And there's a rather broad distribution of  
19 ratios that you see. But the three-quarters power or, you  
20 know, the one-quarter factor, as you see here, is a sort  
21 of midpoint in the range of actual observed differences.  
22 And it says that humans are somewhat more sensitive than  
23 the rodents on a per milligram, kilogram body-weight  
24 basis, but somewhat but not hugely. So that's -- there is  
25 a limited database to support the one-quarter power factor

1 used because of policy --

2 PANEL MEMBER FRIEDMAN: To me that sounds hugely  
3 rather than somewhat if you take that, you know, the  
4 quarter -- the fourth route.

5 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

6 CHIEF SALMON: Well, the possibilities which have  
7 been suggested cover an even wider range. Let's just say  
8 that.

9 You know, the suggestion has been made the  
10 difference in sensitivity might be, you know, all the way  
11 from nothing in the sense that the -- you know, the  
12 effects would be exactly the same on a per milligram,  
13 kilogram body-weight basis, all the way up to the -- you  
14 know, it might be several orders of magnitude higher in  
15 some cases. And there are a few chemicals where clearly  
16 humans are greatly more sensitive than animals. But for  
17 the most part, the difference falls into this range which  
18 is covered by the one-quarter power factor.

19 PANEL MEMBER FRIEDMAN: Thank you.

20 CHAIRPERSON FROINES: Did you want to say  
21 something?

22 PANEL MEMBER HAMMOND: I was just going to say --  
23 I mean I think that also -- surface area is also a scaling  
24 factor as well.

25 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

1 CHIEF SALMON: That was the previous default.  
2 And our original guidelines was the surface area  
3 assumption. That is also broadly consistent with the  
4 underlying data. But there's been a fair amount of  
5 discussion over the last couple of decades as to what is  
6 the best factor. And the sort of consensus position seems  
7 to have coalesced around the one-quarter rather than  
8 one-third choice now. Some of that is not, strictly  
9 speaking, based on the data of relative sensitivity to  
10 carcinogens but rather on the data for various enzymes and  
11 things like that, which seem particularly some of the  
12 xenobiotic metabolizing enzymes seem to cover the range  
13 using a one-quarter rather than the straight surface area  
14 basis. Not that that's a very good -- you know, that's  
15 not a very good reason, but it's one of the things which  
16 factored into the debate.

17 CHAIRPERSON FROINES: We should go ahead. I  
18 realize that these more or less standard scaling factors  
19 or more improved scaling factors are what we always use.  
20 And I was actually making a mistake by asking a question  
21 that was more about metabolism and downstream effects.  
22 And so it's really not particularly relevant to this  
23 particular issue. So let's go ahead.

24 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

25 CHIEF SALMON: We will have further opportunities

1 to discuss this in greater detail in due course, I promise  
2 you.

3           OEHHA STAFF TOXICOLOGIST BROWN: Just to recap  
4 here. We basically have two dose response methods and two  
5 dose metrics. So that's like essentially four  
6 sub-analyses.

7           So if you go to the next slide.

8                               --o0o--

9           OEHHA STAFF TOXICOLOGIST BROWN: This is just a  
10 reminder about the dose -- benchmark dose methodology.

11           Here we're fitting the observed data to a  
12 selection of models. And generally the ones that seem to  
13 fit best are the ones that are similar to the old  
14 multistage polynomial-type model. And we try to identify  
15 a lower bound on a dose that gives a 10 percent  
16 over-the-background response. And essentially that's our  
17 point of departure. And we essentially draw a straight  
18 line between that and the origin or simply divide 0.1 risk  
19 by the lower bound on that benchmark dose and that gives  
20 us a slope or potency.

21           And there's -- generally we've analyzed a large  
22 number of data sets. And frequently the results you get  
23 are very similar to the linearized multistage model. But  
24 there are some differences. The linearized multistage  
25 model is not really designed so fit doses in the upper

1 part of the dose response range. So you can get some  
2 differences, depending upon the data set.

3 And, also, the BMD method places a premium on the  
4 fit of the data. So you generally have a more  
5 stringent -- a fit criteria, a statistical fit criteria  
6 for a choice in model here. But generally that, as you'll  
7 see, the two different dose response methods give similar  
8 results.

9 Next slide.

10 --o0o--

11 OEHHA STAFF TOXICOLOGIST BROWN: Okay. Some more  
12 on our pharmacokinetic assumptions for inhalation in mice.  
13 We used more or less standard response equations here and  
14 in rats. And to estimate low dose inhalation in humans,  
15 we used a pharmacokinetic model with human parameters in  
16 it.

17 Next slide.

18 --o0o--

19 OEHHA STAFF TOXICOLOGIST BROWN: Okay. This is  
20 the first of four slides. There is a graphic coming at  
21 the end, so bear with me here. But this gives the actual  
22 numbers for the five different tumor sites that we  
23 evaluated.

24 In this first slide we're using the linearized  
25 multistage dose response method and the applied lifetime







1 exposure --

2 PANEL MEMBER FRIEDMAN: -- of 10 to the 6 people,  
3 2.4 cases were developed, is that what you mean by that?

4 OEHHA STAFF TOXICOLOGIST BROWN: Yes. You get  
5 2.4 cases if you expose for lifetime at .96 micrograms per  
6 meter cubed, which is the average ambient value in 2005.  
7 So maybe its gone down, hopefully.

8 Next slide.

9 --o0o--

10 OEHHA STAFF TOXICOLOGIST BROWN: We received --

11 CHAIRPERSON FROINES: So 20 million people you'd  
12 have 20 times that number.

13 PANEL MEMBER GLANTZ: So can I just ask one  
14 question before you get on to the comments?

15 OEHHA STAFF TOXICOLOGIST BROWN: Okay. Let's go  
16 back.

17 PANEL MEMBER GLANTZ: In reading through the  
18 thing, in the PBPK model, you know, you have a lot of  
19 parameters you're pulling from various places in the  
20 literature to get the model and I mean that's the way  
21 those models are.

22 But the thing that I sort of kept asking myself  
23 as I was reading it is -- you know, you've got a lot of  
24 knobs you could turn in your predictions. And how  
25 sensitive is your result to the specific values that you

1 use? And how confident are you in them? Because you  
2 didn't really -- you just said here's a number from this  
3 paper and that paper, and sometimes the three or four  
4 significant digits which I always get anxiety attacks  
5 about. But I mean in the end -- I mean the fact that you  
6 ended up with very similar results with the two approaches  
7 was nice. But did you do any sensitivity analysis at all  
8 other than look at the effects of uncertainty in those  
9 parameter estimates

10 OEHHA STAFF TOXICOLOGIST BROWN: Well, you know,  
11 that's an area that we're trying to develop better  
12 techniques. One of the problems with the PBPK modeling is  
13 that you really need better statistical handles for  
14 uncertainty evaluation.

15 Now one of the comments was that the model we  
16 applied was not done in the rat that was used in the  
17 bioassay. It was -- in other words the parameters in the  
18 paper we used for our preliminary modeling was in a  
19 Sprague-Dawley rat, where there actually had been another  
20 publication which we didn't pick up on at the time where  
21 similar modeling, but not exactly the same, slightly  
22 different, was done in the F-344 rat, which we were  
23 actually using the bioassay.

24 So the commenter said, "Well, you've used the  
25 wrong model. And you also used the wrong parameter. You

1 used the human value for the blood air partition  
2 coefficient instead of the rat value," which was, you  
3 know, 60 percent different.

4 Well, you know we didn't think it would make a  
5 big difference. So we went and redid the whole modeling  
6 with the F-344 model, if you like. And there were some  
7 differences at the high dose level, but they really didn't  
8 affect the bottom-line value, what was going on at low  
9 dose, which really determines what the potency's going to  
10 be. So in a sense that was sort of like an uncertainty  
11 evaluation. We used basically two different models and  
12 got similar results, also with two different blood or  
13 partition coefficients, which generally have a stronger  
14 effect on these types of models than other factors.

15 So the short answer to your question is we did  
16 something of that nature. But we hadn't really done a  
17 systematic uncertainty analysis for this. And the actual  
18 number we picked was not actually based on a  
19 pharmacokinetic adjustment.

20 So I think what we're trying to do is develop  
21 models that have better statistical capabilities built  
22 right into the things like Monte Carlo. And we don't have  
23 that yet. The modeling software we have is relatively  
24 rudimentary but it's adequate for a lot of things. But  
25 that's certainly an area where we'd like to see

1 improvement in the future.

2 PANEL MEMBER BLANC: Can I ask a question. It  
3 may not be your bailiwick. But in terms of triggering hot  
4 spot -- a threshold for a hot spot concern, is the current  
5 public policy one case per hundred thousand or one case  
6 per --

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

8 CHIEF SALMON: That's actually a decision which  
9 is made individually by the air districts. And it's the  
10 different air districts do have a somewhat different  
11 policy, depending on their individual circumstances of  
12 the --

13 PANEL MEMBER BLANC: What's the range?

14 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

15 CHIEF SALMON: Typically they start to expect  
16 some kind of action or notification either at 1 in 10 to  
17 the 5th or -- I think the South Coast has a somewhat  
18 higher trigger level because they have high background  
19 levels there. But essentially 1 in 10 to the 5th is the  
20 sort of default starting point. And the level of their  
21 concern obviously rises as the predicted risk goes above  
22 that level.

23 PANEL MEMBER BLANC: And can you just for point  
24 of reference, since we're talking about a cyclic  
25 hydrocarbon, give us the unit risk value -- the predicted

1 risk value -- I'm sorry -- for benzene as it currently  
2 stands?

3 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

4 CHIEF SALMON: Do we have that?

5 OEHHA STAFF TOXICOLOGIST BROWN: I'm going to  
6 have to -- I think we'll have to get back to you on that.

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

8 CHIEF SALMON: Yeah, we'll have -- well, we can  
9 look that up. I don't have it literally to hand at the  
10 moment, but I can look that up.

11 CHAIRPERSON FROINES: Is this room wireless?

12 OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY

13 BRANCH CHIEF MARTY: Yes.

14 CHAIRPERSON FROINES: It's wireless. Then just  
15 go on your website.

16 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

17 CHIEF SALMON: Yeah, we can do that.

18 PANEL MEMBER BLANC: The reason I asked the  
19 questions, because I'm just trying to get a sense of, just  
20 as a logic thing, has this -- where does -- does the value  
21 that you're coming at make some kind of biological  
22 sense -- in terms of biological public health sense in  
23 terms of what one would think was logical? And so I'd  
24 like to see how it plays against -- I don't -- do you have  
25 a cancer unit risk value for -- for the --

1 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

2 CHIEF SALMON: Well, the other two obvious  
3 comparisons are benzene, as you mentioned, and also  
4 perhaps another for naphthalene, which we developed a  
5 little while ago.

6 And this is in the ballpark. It's not -- we're  
7 not hugely far apart. But to give you the exact numbers,  
8 we're going to have to nip off line and do some homework.

9 OEHHA STAFF TOXICOLOGIST BROWN: I think it's  
10 lower than styrene, which is another chemical we worked on  
11 recently. But as Andy said, they're more or less in the  
12 same ballpark.

13 CHAIRPERSON FROINES: Well the methylene chloride  
14 document was -- if you use the applied dose, it was 10  
15 times 10 to the minus 6; and if you use the PK model, it  
16 was 1 times 10 to the minus 6. So it was a factor of 10.

17 PANEL MEMBER LANDOLPH: In the write-up on the  
18 metabolism scheme, Figure 1, which I liked very much, I  
19 wonder if you would consider putting in there some  
20 putative oxygen radical intermediates, some putative  
21 quinones, because you mentioned that you're getting  
22 8-hydroxy-deoxyguanosine and DNA. And you're also getting  
23 some chromosome breakage. And of course the ethyl side  
24 group is influencing the metabolism a lot, pulling it away  
25 from benzene. But there is some comparability there that

1 might be worthwhile just discussing concisely.  
2 Particularly if you're going to use that default linear  
3 no-threshold model, it would give you a little more  
4 justification for doing that.

5 OEHHA STAFF TOXICOLOGIST BROWN: Andy, could you  
6 bring up the metabolism slide at the end.

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION  
8 CHIEF SALMON: Sure, yes.

9 OEHHA STAFF TOXICOLOGIST BROWN: We do actually  
10 have -- it's not in our --

11 CHAIRPERSON FROINES: We can come back to -- I'm  
12 going to raise the same issue. So why don't you go ahead  
13 and we'll come back to it, unless it's coming up next.

14 OEHHA STAFF TOXICOLOGIST BROWN: This is the  
15 slide. This is sort of a classic thing we took out of  
16 Angstrom.

17 And I think you're right in a way. Maybe we  
18 ought to have a second figure that really focuses on this  
19 oxygen and, you know, the quinones and the possibility --  
20 there's a few in the literature of generating a reactive  
21 oxygen species.

22 PANEL MEMBER LANDOLPH: Because you're getting  
23 chromosome breakage in the workers and you're getting, you  
24 know --

25 OEHHA STAFF TOXICOLOGIST BROWN: This is sort of

1 a general slide basically to show the chief urinary  
2 metabolites, the mandelic acid.

3 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

4 CHIEF SALMON: This is the ones which you  
5 actually identified --

6 OEHHA STAFF TOXICOLOGIST BROWN: Right.

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

8 CHIEF SALMON: -- as I understand, rather than  
9 the reactive intermediate --

10 OEHHA STAFF TOXICOLOGIST BROWN: The route at the  
11 bottom, which -- the ring oxidation route leading to  
12 ethylphenol there and also these other suspicious  
13 oxidation products are relatively small metabolites.  
14 These are less than 1 percent generally on the bottom  
15 there.

16 But I think you're right. I think we ought to  
17 have a slide there, because there are a couple that we  
18 could possibly produce that would elaborate a little bit  
19 more in this area.

20 CHAIRPERSON FROINES: Well, as long as we're --  
21 am I interrupting you?

22 Go ahead.

23 PANEL MEMBER LANDOLPH: Just one second.

24 And it would give the document just a little bit  
25 of elegance if you just compared that to benzene. Just a

1 paragraph, a short paragraph would be useful.

2 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

3 CHIEF SALMON: Okay. I think we mentioned it in  
4 our response to comments, but we didn't cover it perhaps  
5 with as much detail as we should in the documents. So we  
6 can add that.

7 Do you want us to proceed with the response to  
8 comments at this point?

9 CHAIRPERSON FROINES: Well, let me just make my  
10 one comment, and then maybe we won't come back to it.

11 I agree with Joe. And I've already told Melanie  
12 that I'm going to bring it up. And, that is, one of the  
13 things that's interesting -- and this is for further  
14 discussion over time -- one of the things that's true  
15 about IARC documents, as you know, is that they now take  
16 into consideration mechanism of action as one of the  
17 criteria for ranking. And it seems to me that that would  
18 be a good approach for us to be taking, and in some  
19 respects we have in the past. And in this case, this  
20 cries out for a brief discussion -- because way back at  
21 the end of your discussion on metabolism and mutations and  
22 what have you, there's this paper by Midorikawa in 2004,  
23 and the thing that's important is he does see oxidative  
24 DNA damage, as Joe just pointed out. But more  
25 importantly, he sees the metabolism -- the metabolites are

1 not those. Those to me are benign. I don't think any of  
2 those are particularly worrisome.

3 But I do think that the ethyl hydroquinone, the  
4 catechol and the quinone are probably the causative agents  
5 for the carcinogenicity, either by reactive oxygen species  
6 generation -- but the ethyl hydroquinone will form  
7 irreversible bonds with amine groups on DNA. And so you  
8 have two possible mechanisms with the quinone -- the  
9 quinone or the catechol, namely, the reactive oxygen  
10 species being formed, which is what the deoxyguanosine  
11 would tend to indicate that you're getting some superoxide  
12 radical anion; and, secondly, that these are going to be  
13 powerful irreversible electrophile inhibitors like  
14 benzoquinone is. Benzoquinone is very active in binding  
15 proteins and DNA.

16 And so I would just give the benzoquin -- the  
17 ethyl benzoquinone a little bit more tension than this one  
18 little paragraph here, because this is the one metabolite  
19 which you can say without any question is potentially  
20 carcinogenic?

21 OEHHA STAFF TOXICOLOGIST BROWN: Well, I believe  
22 there were some in vitro follow-up studies there where  
23 they actually found adducts being formed --

24 CHAIRPERSON FROINES: Yeah, yeah. But I think  
25 I -- rather than putting it at the end sort of buried, I

1 would say mechanism -- potential mechanisms. And those  
2 aren't going to make it in your --

3 OEHHA STAFF TOXICOLOGIST BROWN: Well, actually  
4 that particular paper has a diagram in it which I was  
5 thinking about when you were asking the question. So I  
6 think -- I think we could come up with something that  
7 would expand that graphically with a figure to try to  
8 emphasize a potential mechanism that could support a  
9 linear --

10 PANEL MEMBER LANDOLPH: I agree with that also.  
11 And also the fact that you're finding some chromosome  
12 breakage in the peripheral blood lymphocytes of exposed  
13 workers, that's very similar to what you see with benzene.  
14 And that likely would lead the MOA to segueing from the  
15 oxygen radical generation into the chromosome breakage,  
16 which is how benzene predominantly works.

17 PANEL MEMBER BLANC: I'm not sure -- I understood  
18 your comment to be you're thinking that maybe in addition  
19 to this figure you would put in the other figure?

20 OEHHA STAFF TOXICOLOGIST BROWN: Add another  
21 figure, yes.

22 PANEL MEMBER BLANC: But I actually think it  
23 would be far better for you to take this figure and adapt  
24 it -- you already say that you're adapting it from --

25 OEHHA STAFF TOXICOLOGIST BROWN: Well, it says

1 adapted. Actually it means copied.

2 PANEL MEMBER BLANC: Well, I would suggest it.  
3 Because if you show two different figures with two  
4 different metabolic pathways, it's going to confuse rather  
5 than elucidate. I mean I think you should integrate a  
6 metabolic drawing that is the presumptive metabolic model  
7 that you believe based on best science exists. I'm just  
8 emphasizing what John said. But I have to say that coming  
9 at it as a -- from my end I would be very confused to see  
10 this figure and then another figure which purports also to  
11 be the metabolic pathway, which --

12 OEHHA STAFF TOXICOLOGIST BROWN: The rationale  
13 for this figure is the urinary excretion data, a percent,  
14 you know, of the metabolites comprised with mandelic acid  
15 and so on. I mean those ones across the top, you know,  
16 make up like 95 percent of the actual metabolites  
17 identified in the urine.

18 Now, there are other intermediates and ring  
19 oxidation products which we're concerned about. But I  
20 don't know if it's going to give the right quantitative  
21 idea if we just scrap this thing. Now, I don't know, I  
22 mean we'll certainly --

23 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

24 CHIEF SALMON: -- we'll have to work on that,  
25 yeah, and see what we can --

1           OEHHA STAFF TOXICOLOGIST BROWN: We'll have to  
2 work on that. But I certainly agree we need another  
3 figure to focus on the potential mechanism of action of  
4 these quinones.

5           CHAIRPERSON FROINES: Well, this is important.  
6 And let me give you an example. Roger McClellan in 1983  
7 wrote a paper on putting benzo(a)pyrene on carbon black.  
8 And when they looked at the metabolites, when they looked  
9 at the products after the experiment, and they exposed  
10 animals to them and then looked at the products, what they  
11 found was no products whatsoever from the diol epoxide  
12 that everybody has in every toxicology textbook in the  
13 country. So that what everybody believes is the  
14 mechanistic pathway for the carcinogenesis was BAP going  
15 to a diol epoxide, they found nothing. And they found 20  
16 percent of the benzopyrene quinone.

17           And so one has to ask the question -- you know,  
18 every textbook in the United States has this one pathway  
19 and they didn't find a single bit of evidence.

20           So, when we start to put in metabolism, I think  
21 it's worthwhile to put in information that helps lead you  
22 to your ultimate conclusions. We don't really need review  
23 documents. It's good to have some level of review,  
24 there's no question about that. But I think, and the  
25 Panel may disagree with me, that highlighting those

1 elements of your report that lead to ultimate conclusions  
2 is much more insightful in terms of the Panel  
3 understanding how you got from point A to point Z.

4           PANEL MEMBER LANDOLPH: And that statement on the  
5 summary of the Ethylbenzene genotoxicity I think is  
6 accurate. But I would recommend breaking out into  
7 separating the oxygen radical stuff into a separate  
8 paragraph. So although you correctly point out that  
9 there's no gene mutation in the lower organisms, and some  
10 of the in vitro studies stress, that there is oxygen  
11 radical data, chromosome breakage, which may well be  
12 thought to be the ultimate mechanism by which it had  
13 carcinogenesis or something like that.

14           PANEL MEMBER BYUS: I agree with you because -- I  
15 think you did a very nice job discussing the mechanism of  
16 action in response to the comments, but it's not actually  
17 in the document. So it goes along exactly with exactly  
18 what John says. You want to use that belief of what the  
19 mechanism of action is to lead through the thought  
20 processes on your conclusions. You do it in the comments.  
21 You do it nicely. I think the comments -- it's a very  
22 nice, interesting scientific interchange back and forth  
23 and it's well thought out and I agree with your  
24 conclusions. It's just it's not in the document anywhere  
25 in a logical precise manner, as another paragraph or in

1 conjunction with an additional metabolism slide that  
2 really gets to the crux of the mechanism of action in  
3 terms of metabolism rather than the clearance, which is  
4 part of the PBPK modeling and whatever. And important --  
5 it isn't that important, but it's -- you need to make that  
6 distinction in terms of the amount of the metabolite that  
7 might be responsible for the mechanism of action of the  
8 carcinogenicity. See what I'm saying?

9           So that really just needs to be clearly  
10 documented in the main document. It's all in the  
11 comments, if you care to read it back and forth and find  
12 it. But that's really not where it ought to be.

13           OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

14           CHIEF SALMON: I think our initial approach was  
15 that we would do the -- we would do the unit risk the way  
16 we did it regardless of whether we felt that we knew  
17 what -- that that was the mechanism of action. But having  
18 explored the issue in some length, I think we're coming  
19 around to the view that this is highly plausible even if  
20 we don't feel either the right or the need to absolutely  
21 hang our hat on, as it were.

22           CHAIRPERSON FROINES: Well, you have -- you know,  
23 all of this requires you to be strategic. And when  
24 Melanie is sitting back there and she says, "Oh, my God,  
25 this thing forms a quinone. Froines is going to jump all

1 over us, because that's his pet compound." So you say to  
2 yourself, "Maybe we better put it in the document because  
3 he's clearly going to come back and haunt us on it."

4 Go ahead. I'm sorry.

5 PANEL MEMBER BLANC: This figure that you  
6 adapted, in the adaptation was there -- I assume there was  
7 a label for the lower calicle that was dropped through a  
8 technical --

9 OEHHA STAFF TOXICOLOGIST BROWN: Probably.

10 PANEL MEMBER BLANC: And is that then -- am I  
11 understanding that that as shown is 4-ethylphenol?

12 OEHHA STAFF TOXICOLOGIST BROWN: That's correct.

13 PANEL MEMBER BLANC: And then that 4-ethylphenol,  
14 which is not labeled, is then purportedly on its way --

15 OEHHA STAFF TOXICOLOGIST BROWN: -- on its way to  
16 produce --

17 PANEL MEMBER BLANC: -- to one -- an alternate to  
18 going to glucuronidation as going to this epox -- further  
19 epoxidation and then to a catechol or whatever.

20 OEHHA STAFF TOXICOLOGIST BROWN: A catechol or a  
21 quinone.

22 PANEL MEMBER BLANC: And, therefore, in addition  
23 to the arm that goes to 4-ethylphenol, there's another arm  
24 not shown that we now know goes to 2-ethylphenol?

25 OEHHA STAFF TOXICOLOGIST BROWN: Yes. And that

1 would be the subject of a second slide -- or a second  
2 figure.

3 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

4 CHIEF SALMON: Expansion --

5 OEHHA STAFF TOXICOLOGIST BROWN: -- or expansion  
6 of --

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

8 CHIEF SALMON: -- of this one if we can figure

9 out how to do it.

10 PANEL MEMBER BLANC: You probably -- there's  
11 probably an 18 year old intern on your staff who could --

12 (Laughter.)

13 OEHHA STAFF TOXICOLOGIST BROWN: I'm sure there  
14 is. We need a young brain on this one.

15 PANEL MEMBER BLANC: I mean that's the problem,  
16 right?

17 OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY

18 BRANCH CHIEF MARTY: Yes, it is.

19 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

20 CHIEF SALMON: We have our ways of doing these  
21 things. So we'll have to look at that.

22 PANEL MEMBER BLANC: Or someone's kid maybe.

23 PANEL MEMBER LANDOLPH: Is there any data on  
24 leukemia induction in animals at all? I didn't see any  
25 mention of it. Is there anything in the literature?

1           OEHHA STAFF TOXICOLOGIST BROWN: I didn't come  
2 across that.

3           OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

4           CHIEF SALMON: Are we done on metabolism?

5 Because I just have -- we've managed to do our homework  
6 here, and I just was going to report that we have -- for  
7 benzene we have a unit risk factor of 2.4 times 10 to the  
8 minus 5 per parts per billion or 2.9 times 10 to the minus  
9 5 per microgram per meter cubed, which is about 10 times  
10 the potency of ethylbenzene. And given that there's 3 or  
11 4 parts per billion of benzene in the air, that gives you  
12 actually a background risk of about 1 in 10 to the minus  
13 4. So clearly Benzene is a bigger problem than -- then  
14 this is not a completely negligible problem.

15           PANEL MEMBER BLANC: Good. Well, that's helpful  
16 to me. I don't think that's something that needs to be in  
17 your report, but it's still helpful for me then.

18           OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

19           CHIEF SALMON: But, you know, I'm -- I mean I'm  
20 sorry we didn't have it right away. We should have got it  
21 done.

22           OEHHA STAFF TOXICOLOGIST BROWN: Okay. Let's go  
23 back to the first of the comments slides.

24           We received only one comment, but it was very  
25 voluminous. And so those sort of boil down the responses



1 --o0o--

2 OEHHA STAFF TOXICOLOGIST BROWN: Third one, liver  
3 tumors in female mice are due to increased cell  
4 proliferation and the development of altered hepatic foci.

5 The data supplied showed a weak increase of foci  
6 with females and no effect in males.

7 We OEHHA was not convinced that this potential  
8 MOA is operating or how significant it may be. So we just  
9 thought that was sort of inconclusive.

10 --o0o--

11 OEHHA STAFF TOXICOLOGIST BROWN: And, finally,  
12 lung tumors in male mice are due to the formation of  
13 ring-oxidized metabolites including catechols and  
14 quinones.

15 And our response: It's possible that cytotoxic  
16 quinones may be involved in an MOA for lung cancer, or  
17 possibly other cancers. However, in our view this has not  
18 yet been established. So we just sort of talked about  
19 that possibility, how we should expand on that in our  
20 document. But as yet, we don't have that established mode  
21 of action for any particular --

22 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

23 CHIEF SALMON: I think the commenter's point was  
24 that they were arguing that the quinones were causing  
25 cytotoxicity rather than genetic damage. And that was

1 what we felt was frankly unsubstantiated. And it was as  
2 likely, if not more likely, that the quinones were having  
3 a genotoxic effect.

4 PANEL MEMBER LANDOLPH: Well, they likely do  
5 both.

6 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION  
7 CHIEF SALMON: Absolutely --

8 PANEL MEMBER LANDOLPH: But the key here --

9 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION  
10 CHIEF SALMON: -- as do most full service  
11 carcinogens.

12 PANEL MEMBER LANDOLPH: But in the contest of  
13 carcinogenesis, the genotoxicity is certainly more  
14 important, I think.

15 PANEL MEMBER BLANC: Can you clarify for me when  
16 they kept harping on the term "modified Hill criteria," do  
17 they mean modified Bradford Hill criteria?

18 OEHHA STAFF TOXICOLOGIST BROWN: Yes. Yes,  
19 epidemiological according to --

20 PANEL MEMBER BLANC: Perhaps you could inform  
21 them that Bradford Hill was his full last name and that  
22 Bradford was not his first name, that his name was Austin  
23 Bradford Hill.

24 (Laughter.)

25 PANEL MEMBER BLANC: Or am I missing something?

1 Was there -- has there been some, you know, promulgated  
2 guideline that uses that terminology and has chopped off  
3 his name?

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

5 CHIEF SALMON: No, I think it's a rather  
6 widespread misapprehension. We all know that he was of  
7 course Sir Austin Bradford Hill, the last two being sort  
8 of final names.

9 PANEL MEMBER BLANC: Yeah, Sir is not his first  
10 name either.

11 But thank you, Ethyl, for pointing that out for  
12 me.

13 (Laughter.)

14 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

15 CHIEF SALMON: Ethyl strikes again, yeah.

16 (Laughter.)

17 CHAIRPERSON FROINES: It is true that when I keep  
18 seeing this Hill, Hill, Hill, I wonder if it's some  
19 molecular biologist, you know, down at Cal Northridge or  
20 something. And obviously it's not.

21 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

22 CHIEF SALMON: But not to be confused with author  
23 of the Hill equation either.

24 (Laughter.)

25 OEHHA STAFF TOXICOLOGIST BROWN: I think that's

1 the last slide we have, other than the metabolism slide,  
2 which we sort of chewed over.

3           So I guess we -- if you have additional questions  
4 or comments or suggestions for improving the basic  
5 document, I think we'll go back and address the concerns  
6 you've already mentioned to us and try to come up with a  
7 better figure or figures to --

8           CHAIRPERSON FROINES: Stan.

9           PANEL MEMBER GLANTZ: I just had -- this is sort  
10 of a point I was confused on. If you look on page 14, and  
11 then there's a bunch similar tables following that. I  
12 wasn't sure what -- you have a column there called  
13 "Statistical Significance," and I wasn't quite sure what  
14 you were -- what the hypothesis was.

15           PANEL MEMBER FRIEDMAN: I couldn't figure it out  
16 either. The footnote since explained it. But --

17           PANEL MEMBER GLANTZ: Well, no, I couldn't figure  
18 out the footnote either.

19           PANEL MEMBER FRIEDMAN: Oh.

20           PANEL MEMBER GLANTZ: Oh, okay. Well, then it's  
21 my shortcoming here.

22           But, you know, one of the things, it says their  
23 pairwise comparisons to controls using the Fisher exact  
24 tests. But I presumed that the controls were the ones  
25 that were unexposed.

1 OEHHA STAFF TOXICOLOGIST BROWN: Yes.

2 PANEL MEMBER GLANTZ: So how can you have a P  
3 value for the first line in the table?

4 PANEL MEMBER FRIEDMAN: It says the P value  
5 listed next to the control group is a result of trend  
6 tests.

7 PANEL MEMBER BLANC: You know --

8 PANEL MEMBER GLANTZ: Where did it say that?

9 PANEL MEMBER BLANC: Down below.

10 But, Stan, I had absolutely the same reaction. I  
11 mean I finally understood it. But you really should  
12 not -- there's no hope in the footnotes to help you here,  
13 although they could be a little clearer. But I think that  
14 wherever it is you put the P value for the test for trend,  
15 please don't put it in the first row. It's just  
16 completely confusing.

17 PANEL MEMBER GLANTZ: Yeah, I think you should  
18 just put another line at the bottom that says test for  
19 trend or something.

20 PANEL MEMBER BLANC: And each of the tables has  
21 that. It was completely --

22 PANEL MEMBER GLANTZ: Yeah, that's right. I was  
23 totally -- well, at least one member of the panel was  
24 smart.

25 PANEL MEMBER FRIEDMAN: Well, that was one of the

1 few things that I was very concerned about too. But I  
2 just read the footnote and I finally understood --

3 OEHHA STAFF TOXICOLOGIST BROWN: You just  
4 happened to read the footnote and find --

5 PANEL MEMBER FRIEDMAN: Yeah. Well, so I mean --  
6 so I agree with better communication now.

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION  
8 CHIEF SALMON: We will clarify that.

9 PANEL MEMBER GLANTZ: Well, I read the footnote  
10 too and I completely didn't get it.

11 So, anyway, the other thing about this table and  
12 the others is I think it would just be helpful in kind of  
13 thinking about the dose response -- and then this actually  
14 is a whole bunch of places in the report where you do  
15 this -- where you have the tumor incidents and, for  
16 example, for the controls you have 3 over 42 and for 750  
17 ppm it's 21 over 36, I think it would be helpful to add  
18 another column that just has what that ratio is. You see  
19 what I'm saying? Take out the calculator and figure it  
20 out. Because that -- I mean I think you want to keep what  
21 you've got because it shows you, you know, the actual  
22 numbers, which I think is important. But just adding --  
23 and this applies to the other tables -- you know, just so  
24 you don't have to take out your calculator.

25 PANEL MEMBER LANDOLPH: And in that footnote for

1 tumor incidents, under D, could you just define that as  
2 total number of tumors over total number of animals, just  
3 to be brutally clear.

4 PANEL MEMBER GLANTZ: In other words, presented  
5 this way, two out of three panel members were confused?

6 PANEL MEMBER FRIEDMAN: I was -- the third one  
7 was too.

8 PANEL MEMBER GLANTZ: But you figured it out.  
9 So two out of three were terminally confused.

10 OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY

11 BRANCH CHIEF MARTY: That's 66.67 percent.

12 (Laughter.)

13 PANEL MEMBER HAMMOND: It was the 95th  
14 percentile.

15 PANEL MEMBER FRIEDMAN: You were really good  
16 about defining your abbreviation, but you didn't define  
17 NTP, at least that I could find. So I didn't know what it  
18 was until I found the reference.

19 OEHHA STAFF TOXICOLOGIST BROWN: That's true.

20 PANEL MEMBER FRIEDMAN: And then I would just  
21 like to suggest you could -- it took me a minute to figure  
22 out what MO -- it may be everybody here knows exactly what  
23 MOA is. But it took me a minute to figure out it was  
24 mechanism of action. So I'd like to do -- try to avoid  
25 these action items.

1           OEHHA STAFF TOXICOLOGIST BROWN:  Okay.  Let's do  
2 a jargon hunt to make sure we have --

3           PANEL MEMBER HAMMOND:  -- have in place  
4 jargonisms.

5           (Laughter.)

6           PANEL MEMBER GLANTZ:  Yeah.  I absolutely had the  
7 same thing with MOA where I actually guessed what it was.

8           PANEL MEMBER FRIEDMAN:  Ah, you see.  So  
9 sometimes --

10          PANEL MEMBER GLANTZ:  If you're given enough  
11 monkeys and enough typewriters.  But, yeah, I agree.  I  
12 think --

13          OEHHA STAFF TOXICOLOGIST BROWN:  NTP is  
14 identified in the references, by the way.  So if you got  
15 that far --

16          PANEL MEMBER FRIEDMAN:  I finally found it there.  
17 But --

18          PANEL MEMBER GLANTZ:  Well, I had the same thing  
19 with LTWA.  I had to kind of look around to figure out  
20 what that was.

21          OEHHA STAFF TOXICOLOGIST BROWN:  Okay.  We'll try  
22 to fix those deficiencies.

23          PANEL MEMBER LANDOLPH:  You know, but I want to  
24 say overall I liked the report.  These are things that can  
25 sharpen up.  I think it's written very well.  It's done

1 competently. It's got a lot of the correct background  
2 literature. So I was very pleased with the document in  
3 general.

4 PANEL MEMBER BLANC: Are these your comments,  
5 Joe?

6 PANEL MEMBER LANDOLPH: Yeah. I forgot to sign  
7 them.

8 CHAIRPERSON FROINES: Does the Committee want to  
9 approve the document pending changes, or do you want to  
10 delay a vote until you see the next --

11 PANEL MEMBER BLANC: No, no. I'll be happy to  
12 make the motion that we approve this document as  
13 submitted, presuming the minor changes are made.

14 PANEL MEMBER LANDOLPH: I'll second.

15 CHAIRPERSON FROINES: Conversation, comments?

16 All in favor?

17 (Ayes.)

18 (Hands raised.)

19 CHAIRPERSON FROINES: The vote is unanimous for  
20 approval of the document on ethylbenzene.

21 Want to take a break?

22 THE REPORTER: No, I'm fine.

23 CHAIRPERSON FROINES: That went by so easy, it  
24 was disappointing.

25 OEHHA STAFF TOXICOLOGIST BROWN: After 20 years

1 on this, we're getting better at it.

2 (Laughter.)

3 CHAIRPERSON FROINES: Do you want to take a quick  
4 break?

5 PANEL MEMBER BLANC: Yes, sure.

6 CHAIRPERSON FROINES: Okay. Five minutes.

7 (Thereupon a recess was taken.)

8 CHAIRPERSON FROINES: May we reconvene?

9 Drs. Glantz, Salmon, Friedman, Hammond.

10 In my office we have a jar. And if you use a  
11 colloquialism, you have to put a quarter in for an  
12 end-of-the-year party.

13 (Laughter.)

14 CHAIRPERSON FROINES: So we should have a jar for  
15 people who don't come back to the table at the end of the  
16 break.

17 PANEL MEMBER LANDOLPH: Do we get to take money  
18 out if we come back early?

19 (Laughter.)

20 CHAIRPERSON FROINES: Great.

21 Tobi.

22 PANEL MEMBER GLANTZ: Are you an economist too?

23 PANEL MEMBER LANDOLPH: No, just poor, just poor.

24 (Laughter.)

25 PANEL MEMBER HAMMOND: Just a professor at UC.

1           CHAIRPERSON FROINES: Thank you, Tobi.

2           DPR ASSISTANT DIRECTOR JONES: I'm Tobi Jones,  
3 Department of Pesticide Regulation. I want to thank the  
4 Chair and members of the Scientific Review Panel for  
5 providing DPR the opportunity to present our risk  
6 assessment on endosulfan and our proposal to list  
7 endosulfan as a toxic air contaminant.

8           Endosulfan is one of the few organoinsecticides  
9 remaining in use in the U.S. While endosulfan's use  
10 continues to decline, it is still a preferred insecticide  
11 for certain crop pest combinations in California. This  
12 continued use means that there is still sufficient ambient  
13 air exposure to warrant endosulfan as a toxic air  
14 contaminant.

15           DPR is aware of a recent report by the Department  
16 of -- California Department of Public Health on the  
17 association of the use organochlorine pesticides,  
18 including endosulfan, with cases of autism, and we will  
19 work with Department of Public Health on this issue.

20           Since DPR's public comment period on endosulfan  
21 ended late in August, we have not completed our responses  
22 to the received comments. We will provide those comments  
23 and our responses to the Panel in the near future.

24           I'd like to turn this over to the three DPR staff  
25 who are authors of the risk assessment. Dr. Shifang Fan

1 will present the environmental fate and use of endosulfan.  
2 Dr. Sheryl Beauvais will discuss the assessment of  
3 exposure to endosulfan. And Dr. Marilyn Silva will  
4 discuss the human health assessment and conclusions about  
5 the proposal to list endosulfan as a toxic air  
6 contaminant.

7 CHAIRPERSON FROINES: Welcome.

8 (Thereupon an overhead presentation was  
9 Presented as follows.)

10 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

11 FAN: The environmental fate of endosulfan.

12 Endosulfan is a pesticide belonging to the  
13 chemical family of organochlorine, and the sub-class  
14 chlorinated cyclodiene, with only one double bond. Its  
15 molecular structure has two stereochemical isomers,  
16 alpha-endosulfan and beta-endosulfan. The alpha-endo  
17 isomer is asymmetric; the beta-endosulfan is symmetric.

18 --o0o--

19 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

20 FAN: Endosulfan is poorly soluble in water, but  
21 readily soluble in common organic solvents.

22 Alpha-endosulfan has higher vapor pressure, so it's more  
23 volatile. And the beta-endosulfan has higher adsorption  
24 coefficient. Therefore there's more affinity onto soil  
25 particles.

1 --o0o--

2 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

3 FAN: Endosulfan is a broad-spectrum non-systemic  
4 insecticide and acaricide with contact and stomach action.  
5 It is used to control sucking, chewing, and the boring  
6 insects on a wide variety of vegetables, fruits, cotton,  
7 and trees. Currently, there are six registered products  
8 containing active ingredient of endosulfan in California.  
9 Formulations include emulsifiable concentrate, wettable  
10 powder, and the technical grade endosulfan. The technical  
11 grade endosulfan is used to formulate the end-use  
12 products. All labels bear a signal word "Danger" and  
13 "Poison." It is a restricted pesticides in California.

14 --o0o--

15 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

16 FAN: In recent ten years, annual endosulfan use  
17 decreased from more than 200,000 pounds in 1997 to about  
18 83,000 pounds in the year 2005. The 2005 is the latest  
19 year when the use data was completely compiled.

20 --o0o--

21 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

22 FAN: Here is Endosulfan use distribution map.  
23 The top use counties are Fresno, Kings, Imperial, Kern,  
24 Tulare, and the Riverside in San Joaquin Valley and the  
25 Imperial Valley.

1           CHAIRPERSON FROINES: Does anybody look for it in  
2 the Colorado River?

3           DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

4           FAN: Pardon?

5           Colorado River, no.

6           Sorry. It takes a while for the next slide  
7 because it's the map side-by-side comparison.

8                               --o0o--

9           DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

10          FAN: This side-by-side comparison of use map  
11 with the same scale showed the decreased endosulfan --

12          PANEL MEMBER GLANTZ: Could you back up?

13          DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

14          WOFFORD: It's taking a while to get back to it.

15          DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

16          FAN: Okay. That map has the same scale, shows  
17 that decreased Endosulfan use in 2005 was mainly due to  
18 reduction of the cotton crop in the San Joaquin Valley.

19                               --o0o--

20          DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

21          FAN: This monthly use for the entire state

22 showed that the peak use months were from June to  
23 September. For the top six use counties the peak use  
24 months varied from county to county within June to  
25 September.

1                               --o0o--

2               DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

3               FAN: In California, endosulfan was mainly used  
4 on cotton, alfalfa, lettuce, tomato, and the melons.

5                               --o0o--

6               DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

7               FAN: Endosulfan fate. The physicochemical  
8 properties of endosulfan determine its fate in  
9 environment. The fate here includes inter-environmental  
10 media transportation and the inner-media transformation.

11               Endosulfan is released to the environment almost  
12 exclusively from pesticide applications. And there is no  
13 known natural source of Endosulfan. But it was found in  
14 almost all environmental media and all over the world. As  
15 we mentioned previously, the alpha-endosulfan is more  
16 volatile and the beta-isomer is more adsorptive and  
17 persistent. It's overall moderately volatile property  
18 enables it to be transported as vapor and spray drift to  
19 multiple media. Its moderately adsorptive and persistence  
20 properties enable it to stay in the environment for an  
21 extended period and it can be transported via runoff to  
22 the surface water bodies or via dust dispersion to  
23 atmosphere and the redeposit to off-target areas.

24               Therefore, Endosulfan has been detected in areas  
25 where it was never used, such as Lake Tahoe Basin and

1 Sequoia National Park, and even in the Arctic.

2           Endosulfan degradation come via biotic or abiotic  
3 process in aerobic and anaerobic conditions. Both alpha-  
4 and the beta-endolsulfan can be oxidized to endosulfan  
5 sulfate via biotic metabolism. Endosulfan sulfate is of  
6 comparable toxicity as its parents and more persistent.  
7 They all can hydrolyze abiotically or biotically to  
8 endosulfan diol. Endosulfan diol is more hydrophilic and  
9 less toxic. They can be further metabolized to various  
10 intermittent metabolites and eventually mineralize to  
11 release carbon dioxide. But the processes are slow.  
12 Therefore, most common chemical forms found in the  
13 environment are alpha- and beta-endosulfan, endosulfan  
14 diol, and endosulfan sulfate. Alfa- and beta-endosulfan  
15 and the endosulfan sulfate are toxicity concerns.

16                                   --o0o--

17           DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

18           FAN: In soil. Adsorption immobilizes the  
19 endosulfan to be leached to groundwater. So leaching is  
20 not important. However, both dissolved and the  
21 particle-bounded endosulfan can be transported via runoff  
22 to rivers and lakes and eventually to the ocean.

23           Endosulfan can volatize to the atmosphere from  
24 the soil water surface driven by Henry's Law constant.  
25 Study showed that approximately half of the amount of

1 endosulfan applied to surface soil was lost via  
2 volatilization in three to five days for alpha-endosulfan  
3 and five to eight days for beta-endosulfan. Endosulfan  
4 bounded on soil particles can also be transported as dust  
5 to the atmosphere from dry soils.

6 Endosulfan degradation in soils depends on many  
7 factors, such as soil type, organic carbon content, pH,  
8 temperature, moisture content, microbial population, and  
9 the biomass. Reported half-lives vary from 28 days to  
10 more than 200 days and typically it's 50 days.

11 --o0o--

12 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

13 FAN: Endosulfan contaminated to -- okay, in  
14 water. Endosulfan contamination to surface water bodies  
15 is mainly due to spray drift and the runoff  
16 transportation. Spray drift consists alpha- and  
17 beta-endosulfan from applications. Runoff events can  
18 carry all three types of toxic endosulfan. And most  
19 likely to be dominated by endosulfan sulfate due to its  
20 more persistence.

21 Endosulfan loss from water involves adsorption  
22 and volatilization. In a laboratory study, 24 hours  
23 evaporation at room temperature resulted in 26 to 27  
24 percent of alpha-endosulfan loss, but 95 to 98 beta  
25 endosulfan remained in the incubation vials.

1           Endosulfan hydrolysis favors in neutral to  
2 alkaline water. Half-lives varied from hours to more than  
3 200 days, depending on pH and temperature. At acidic  
4 water, oxidation becomes the main degradation process.

5                           --o0o--

6           DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

7           FAN: In atmosphere. Volatilization and the  
8 vapor transportation are the main processes for the  
9 endosulfan entering to and moving in the atmosphere. When  
10 endosulfan is applied onto crop, volatilization starts and  
11 the vapor is transported by wind and turbulence. The  
12 continuous volatilization and the vapor transportation  
13 eventually remove up to 50 to 70 percent of total  
14 endosulfan deposit on the crop surface. Volatilization  
15 from soil solution and free water surface also contributes  
16 to the atmospheric endosulfan but at much lower rates.

17           Spray drift can result in endosulfan  
18 intentionally moved to off-target areas. There were many  
19 spray drift events reported in eighties and nineties. The  
20 spray drift is manageable via regulations and the  
21 technical improvement.

22           Another source of atmospheric endosulfan is from  
23 dust dispersion and transportation. Its importance  
24 depends on regional weather, geographic and topography  
25 conditions, and human activities. Dust transport can

1 carry all three toxic forms of endosulfan, but much lower  
2 in magnitude than spray drift and the vapor transport.

3 CHAIRPERSON FROINES: Question. I have just one  
4 question.

5 I wasn't quite clear on your spray drift. You  
6 then say manageable. And I wasn't sure what you meant by  
7 that.

8 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

9 FAN: Let me give you -- in 1988, the California  
10 Department of Food and Agriculture monitored aerial  
11 application of endosulfan to three fields in the most 19  
12 drainage area in Monterey County. Endosulfan was found on  
13 deposit sample location 18 feet from the application  
14 field. This information was used to develop education  
15 measure to reduce off-site movement of endosulfan.

16 And the U.S. EPA started the 300 feet of buffer  
17 zone. And California Pesticides Regulation Department  
18 have like a certain times to have some regulations, and  
19 certain time you can spray and, you know, what kind of  
20 wind or the weather conditions you can spray. And if the  
21 wind exceeds some criteria, and then you cannot spray.  
22 Something like that, the regulation managing the spray  
23 drift.

24 And the technical improvement I think of the  
25 aircraft type and the nozzle and the drop letter size, all

1 that, have some experimental data and that they set some  
2 regulations for that.

3           PANEL MEMBER BLANC: I think what Dr. Froines is  
4 getting at is that you're mixing two different issues. If  
5 you're presenting the technical atmospheric fate data,  
6 then clearly it's easily entering into the atmosphere via  
7 drift. Whether or not there may be administrative  
8 recommendations in order to reduce that problem is an  
9 editorial comment, which I don't think belongs in the  
10 environmental fate. The environmental fate is not that  
11 because this is a big problem, there have been a number of  
12 regulations that have been introduced. The environmental  
13 fate is that it easily is distributed through drift, end  
14 of story. I mean you could say because of that various  
15 regulations. But if you just say, "and that's a  
16 manageable problem," well not really. It seems like it's  
17 a problem that's substantive enough that there have been  
18 all of these steps that have been recommended. And since  
19 we all know that things that are recommended may not  
20 happen, and since you're talking in general terms -- I  
21 mean I hope I'm not putting words in your mouth, but I  
22 think that's where you were going with this comment.

23           CHAIRPERSON FROINES: I think it's a potential  
24 can of worms to get into that discussion of what somebody  
25 means by manageable, because then you have to deal with

1 the issue of evaluation and validation, and that's really  
2 out of the scope of this discussion. So we --

3 PANEL MEMBER BYUS: I have another question  
4 though.

5 So when you spray -- so I just want to get clear  
6 in my mind the difference between drift and  
7 volatilization, and then what happens to that volatile  
8 chemi -- what happens to endosulfan once it's volatilized?

9 So I imagine you mean by drift, you're talking  
10 about during the spraying process, actual drift of the  
11 particulate spray?

12 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

13 FAN: That is one thing that happens in the  
14 application.

15 PANEL MEMBER BYUS: During application.

16 But the volatilizations, so you're saying that 50  
17 to 70 percent of what is sprayed on plants doesn't stay on  
18 the plant, it goes back up into the air through --

19 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

20 FAN: Yeah, because of the -- they volatilize  
21 from the -- surface and turbulence and the wind dilutes  
22 the -- took away and then volatilization continues. There  
23 is probably in a few days -- in two to three days. That  
24 depends on the weather and two to three days or three to  
25 five days, yeah, probably 70 percent -- 50 to 70 percent

1 will eventually volatilize from the surface of the crop.  
2 That I got from the literature.

3 PANEL MEMBER BYUS: But that's not considered  
4 part of your actual drift concern?

5 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

6 FAN: It's not drift. It's volatilization. It's  
7 volatilization.

8 PANEL MEMBER BYUS: And the reason is because  
9 it's more diluted, is that the -- I mean --

10 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

11 FAN: The volatilization is their -- their  
12 property. But if the weather condition -- if the wind  
13 turbulence is strong and then if -- it moves away fast and  
14 then comes in. The volatilization is also driven by  
15 the -- because -- if continue to dilute, they will  
16 continue to volatilize if the partial pressure here is  
17 high and the volatile is lower. But it's already diluted  
18 and it's -- it's low, but it's high and fast.

19 PANEL MEMBER BYUS: Okay. So let me ask -- I  
20 guess the question that we ask is --

21 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

22 FAN: The volatilization is just like the  
23 dissolution in the water. It's driven by the  
24 concentration. Though for the air it's driven by the  
25 partial pressure I think.

1           PANEL MEMBER BYUS: Right. But say you were  
2 standing next to a field that had been sprayed and you  
3 were downwind of it for the next day, say you lived 50 --  
4 or beyond the 300 feet, would it blow down in your  
5 direction following the volatilization? Would it be a  
6 significant exposure to you, to someone?

7           DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

8           FAN: They do 300 feet, I think they'd probably  
9 have the data support it.

10          DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

11          WOFFORD: Sheryl will be talking about that  
12 later.

13          PANEL MEMBER BYUS: Right. But I mean that's  
14 what -- I'm just trying to get this straight in my mind,  
15 when you're talking about the environmental plate and the  
16 drift versus volatilization and we talk about exposure,  
17 where all this falls.

18          DPR ASSISTANT DIRECTOR JONES: This is Tobi  
19 Jones. Let me just see if I can clarify.

20                 I think within DPR in our regulatory structure we  
21 use spray drift terminology exactly as you indicate, Dr.  
22 Byus. And that is off-site movement during or as a result  
23 of application. If after material has settled on to plant  
24 or soil surfaces and it then volatilizes off, we're not  
25 currently calling that drift.

1           And I would say to the Committee, there's  
2 currently a discussion with environmental groups about  
3 that definition of drift as regulators use it, not just  
4 DPR but also U.S. EPA.

5           So I think what you have surmised from this is  
6 the case, that we're -- for the environmental fate of  
7 endosulfan, Shifang is talking about the material that  
8 comes off after the application, not during the  
9 application. And I think that's where her terminology on  
10 spray drift during the application being manageable by the  
11 kinds of technologies that she described is the case.

12           DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

13           WOFFORD: Yeah, and Sheryl later will be giving  
14 results of an ARB study done. And actually concentrations  
15 after the application were higher in the air than during  
16 application. So as the volatilization is more --

17           CHAIRPERSON FROINES: I would argue that this is  
18 an issue that -- I mean you put your finger on what is a  
19 contentious issue and that there is a current policy, as  
20 Tobi just said. But this is, for example, particularly  
21 problematic when we get to fumigants like Telone, where  
22 it's injected into the soil, and as it vaporizes out of  
23 the soil and ends up in urban areas, do you call that  
24 drift or do you call that just happening to, you know,  
25 blow that way?

1           So I think that when you have something like a  
2 fumigant where it volatilizes and ends up in Bakersfield,  
3 I think one's going to have a hard time not calling that  
4 drift. And so this is an issue which I think we don't  
5 need to pursue today, but it's a policy issue of some  
6 consequence.

7           Go ahead.

8           PANEL MEMBER GLANTZ: If I can -- Because I  
9 remember a very hot meeting with DPR in San Diego a long  
10 time ago where there was a huge fight about this. But I  
11 think though that you are saying, whether you call it  
12 drift or banana, that this stuff is moving off site as a  
13 result of its application -- even if it is applied  
14 correctly and in accordance with the current standards, it  
15 moves off the site. But what you call that movement, you  
16 know, but it is moving off, you know. If it's blown off  
17 while it's being applied, that's one way to move off. But  
18 you're saying even if it doesn't blow off while it's being  
19 applied, it's going to volatilize and the volatilized  
20 stuff is going to blow off. So what you call it -- I  
21 never quite could figure out why this was such a hot  
22 issue. But it's clearly moving all over the place.

23           DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

24           FAN: They both move the toxic to off-site areas.

25           PANEL MEMBER GLANTZ: Right.



1 FAN: In atmosphere. Endosulfan is not  
2 susceptible to atmospheric degradation. The cloud  
3 droplets and the rainwater usually are acidic. Therefore,  
4 hydrolysis is not a common process in atmosphere.  
5 Endosulfan does not absorb --

6 CHAIRPERSON FROINES: I'm sorry to interrupt you  
7 again. I don't mean to be rude.

8 The lead for exposure on this Committee was  
9 Kathy. And so -- and Roger's usually the person who deals  
10 with atmospheric chemistry. So I assume that since you're  
11 not raising a complaint, that you're comfortable --

12 PANEL MEMBER HAMMOND: No, I assumed that the  
13 fate was being -- that was assigned to someone else, I  
14 thought.

15 CHAIRPERSON FROINES: Jim.

16 PANEL MEMBER HAMMOND: Well, I thought that's  
17 what you just said. So I didn't do fate.

18 I thought I was doing exposure, which is --

19 CHAIRPERSON FROINES: Was Roger to look at this  
20 point?

21 PANEL LIAISON BEHRMANN: This is Jim Behrmann,  
22 liaison to the Panel.

23 No, we only assigned two leads in this -- for  
24 this report, exposure and health. And so if there's a  
25 miscommunication, I apologize. You know, we did not --

1 PANEL MEMBER HAMMOND: That's my fault then --

2 PANEL LIAISON BEHRMANN: -- I did not assign fate  
3 specifically to Dr. Hammond.

4 CHAIRPERSON FROINES: So we will get -- we will  
5 have to do findings on this chemical at the next meeting.  
6 So in the interim we can deal with the photolysis. So  
7 that -- oh, I'm not saying you're wrong. I'm simply  
8 saying the Panel should review the photolysis -- the  
9 atmospheric chemistry issue, and it hasn't been done by  
10 us.

11 PANEL MEMBER HAMMOND: My fault.

12 PANEL LIAISON BEHRMANN: I apologize. It was my  
13 error in not clarifying that with Dr. Hammond. So we can  
14 work with Dr. Atkinson to, you know, also do that.

15 CHAIRPERSON FROINES: All right.

16 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

17 FAN: Endosulfan does not absorb solar radiation  
18 of the troposphere, so photolysis can also be negligible.

19 Indirect photo-oxidation with hydroxyl radical  
20 may result in endosulfan sulfate and endosulfan diol  
21 susceptible to photolysis. However, they are not abundant  
22 in the atmosphere. Therefore, half-life was estimated to  
23 be 1.5 years for alpha-endosulfan.

24 --o0o--

25 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

1           FAN: Air concentration of endosulfan.  
2 Endosulfan concentration in air depends on the distance  
3 from the application sites. For short-range  
4 transportation, seasonal variation typically mirror the  
5 agricultural practice. Temperature and the application  
6 frequency mainly drive the air concentration in the area.  
7 For regional range, the joint U.S. EPA and the Environment  
8 Canada monitoring project investigated atmospheric toxic  
9 contaminants to the Great Lakes region. The vapor phase  
10 results showed a distinct annual cycle with peaks in  
11 summer one or two orders of magnitude higher than in  
12 winter. Summertime average concentrations was 80  
13 picograms per cubic meter for alpha-endosulfan.  
14 Concentrations for beta-endosulfan and the endosulfan  
15 sulfate were generally lower. For long distance  
16 transportation to the Arctic, average air concentrations  
17 ranged from 1 to 10 picograms per cubic meter. As part of  
18 Toxic Air Contaminant program, Department of Pesticides  
19 Regulation provided endosulfan use report and the air  
20 monitoring recommendations to Air Resources Board for  
21 documenting the airborne endosulfan concentrations.

22           ARB monitored an endosulfan application in San  
23 Joaquin County in 1997, and conducted an ambient air  
24 monitoring in Fresno County in 1996.

25           Our next speaker, Sheryl, will present more

1 details for these monitoring studies.

2 --o0o--

3 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

4 FAN: Here is just a brief summary of the ARB's  
5 monitoring results. For application monitoring of total  
6 28 samples, 96 percent had alpha-endosulfan above the  
7 quantification limit. The highest individual  
8 concentration was 38 nanogram per cubic meter. Only 57  
9 percent sample had beta-endosulfan above the  
10 quantification limits. The highest concentration was 200  
11 nanogram per cubic meter. Endosulfan sulfate was detected  
12 in 7 out of 28 samples, but less than the quantification  
13 limits.

14 For ambient monitoring study, of total 75 samples  
15 reported, 88 percent had alpha-endosulfan above the  
16 quantification limits. And the highest one-day  
17 concentration was 140 nanograms per cubic meter. Only 3  
18 percent samples had beta-endosulfan greater than the  
19 quantification limits. And the highest one-day  
20 concentration is 26 nanograms per cubic meter.

21 PANEL MEMBER FRIEDMAN: Could you explain what  
22 the LOQ and LOD are? I don't quite understand that.

23 MR. FRANK: Okay. LOQ is limit of  
24 quantification. LOD is the limit of -- detection limit.

25 PANEL MEMBER FRIEDMAN: What does that mean?

1 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

2 FAN: The use of the -- is the instrument -- the  
3 smallest amount in the instrument that can detect it. If  
4 they can't detect it, they cannot quantify it --

5 PANEL MEMBER FRIEDMAN: You mean because it's so  
6 high --

7 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

8 FAN: -- reliably. So they set it -- sometime  
9 they set it at 1 to 5 times of the LOD. So they feel  
10 confident it can reliably quantify. But that the  
11 measurable amount is just the same. So LOD and LOQ is the  
12 same. But for the endosulfan I think it's different.

13 PANEL MEMBER HAMMOND: No, it couldn't be the  
14 same if you have --

15 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

16 FAN: No, this one is not. For some chemicals.

17 PANEL MEMBER HAMMOND: Oh, for some. Okay.

18 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

19 FAN: Yeah.

20 PANEL MEMBER HAMMOND: Yeah, here it's not?

21 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

22 FAN: For this one it's not, right.

23 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

24 WOFFORD: Yeah, the one level is the level they  
25 can actually -- they'll see within their blip on their

1 thing. And the other one is where they can actually  
2 quantify. So in between those two levels there's kind of  
3 a gray area where they know it's there, but they can't  
4 give you a quantifiable amount.

5 PANEL MEMBER FRIEDMAN: So they're both low?

6 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

7 WOFFORD: Yeah.

8 PANEL MEMBER FRIEDMAN: One is so low you

9 can't --

10 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

11 WOFFORD: Right.

12 PANEL MEMBER FRIEDMAN: -- and the other is so

13 low you can't be sure of it?

14 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

15 WOFFORD: But we know there's something there,

16 but they can't measure it.

17 PANEL MEMBER BLANC: So I'm confused. Someone

18 else is going to be presenting in more detail the sampling

19 data?

20 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

21 WOFFORD: Um-hmm, Sheryl will --

22 PANEL MEMBER BLANC: And that's the next speaker?

23 PANEL MEMBER BYUS: Right.

24 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

25 FAN: She will give you more detail about how to

1 correct the data, how to --

2 PANEL MEMBER BLANC: I just want to make an  
3 observation though. We have a hundred samples on which  
4 we're basing the data. Is that all the sampling we're  
5 going to hear about?

6 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

7 WOFFORD: For the assessment, yeah.

8 PANEL MEMBER BLANC: So we have approximately one  
9 sample for every 15,000 pounds of this toxin that's been  
10 used over the last ten years?

11 There's on average 15,000 pounds used per year,  
12 or is it 150,000 pounds used per year based on your  
13 previous slide?

14 CHAIRPERSON FROINES: 2004 was 150,000 pounds.

15 PANEL MEMBER BLANC: Right.

16 PANEL MEMBER HAMMOND: But now it's greatly  
17 reduced from before.

18 PANEL MEMBER BLANC: I understand that. But the  
19 last samples you have are from 1996 and 1997, and  
20 altogether we have 100 samples that we've had ten years of  
21 use in the interval, have at least 150,000 pounds a year.  
22 So we approximately have one sample per every 150,000  
23 pounds.

24 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

25 FAN: Oh, this use not the way. This is just the

1 sample taken from one study -- one application, one  
2 ambient study.

3 PANEL MEMBER BLANC: So we'll be hearing --  
4 that's why I asked. Are we about to hear about other  
5 sampling as well?

6 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

7 WOFFORD: It's going to be the ARB sampling that  
8 was done. That's where we're going to get the results the  
9 assessment are made on.

10 PANEL MEMBER BLANC: So why did you present these  
11 sampling data here? What was the purpose of these  
12 sampling data if you're about to --

13 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

14 WOFFORD: That was a summary of the ARB sampling  
15 that was done. And Sheryl will be giving you more  
16 in-depth concentration --

17 PANEL MEMBER BLANC: -- of the same hundred  
18 samples?

19 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

20 WOFFORD: Yes.

21 PANEL MEMBER BLANC: So we have a hundred samples  
22 over ten years in total, that's all our sampling?

23 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

24 WOFFORD: Yeah.

25 PANEL MEMBER BLANC: I just want to be clear.

1 But I'll make my critique on that later. I just want to  
2 make sure --

3 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

4 WOFFORD: This one is done completely on the ARB  
5 study that was done.

6 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

7 FAN: We only do one sample for ten years. But  
8 some other people did a lot of studies.

9 PANEL MEMBER BLANC: In other states?

10 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

11 FAN: Yeah.

12 CHAIRPERSON FROINES: Joe.

13 PANEL MEMBER LANDOLPH: Yeah, I was also assigned  
14 to help out on this document too, mostly the health  
15 effects, I'm sure.

16 This third volume I thought was written pretty  
17 well. I particularly liked that figure 10 on the  
18 degradation in the water.

19 One comment I would make is, throughout not only  
20 Volume 3 but the other volumes, if you could include some  
21 concise discussion of the enzymes that metabolize  
22 endosulfan in bacteria and in mammals, that would be very  
23 helpful, because there's a lot of metabolites but there's  
24 no enzymology and that's sorely lacking. So if you could  
25 add that in 3 and in the other volumes, that would be very

1 helpful.

2 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

3 FAN: Yes. I think that's a very good point.

4 We'll address that when we do the revision for the final.

5 PANEL MEMBER LANDOLPH: I have to apologize for  
6 not getting my comments to you earlier. You sent me the  
7 first volume and then he said, "Don't do this one. We're  
8 going to send you a second copy." And then it got buried  
9 under a blizzard of paper.

10 CHAIRPERSON FROINES: I just wanted to -- I'm  
11 curious as to -- I'm looking forward to the next  
12 presentation, because the numbers that were on the screen  
13 were not the numbers that you actually said.

14 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

15 WOFFORD: The numbers she gave were actually  
16 summations between the different isomers. So you're --

17 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

18 FAN: What, this one?

19 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

20 WOFFORD: Yeah, the ones you composed.

21 CHAIRPERSON FROINES: Those two numbers that are  
22 on the screen were never mentioned in what you said. They  
23 were other numbers. And so as far as I know, I have no  
24 idea what anything is at this point.

25 Am I --

1 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

2 FAN: This one is not a concentration. Because  
3 Sheryl will talk about your detail about a concentration.  
4 I just give the summaries how many samples we have taken  
5 and how many above the quantification limit, that there is  
6 96 percent. I didn't put a lot of column here because I  
7 don't want to have the whole slide full of the numbers and  
8 confuse people. Actually this way you have to have a  
9 calculator.

10 So 96 percent of 20 -- I do have it -- 27 out of  
11 28 is above the quantification limit that's spent for  
12 95 -- 96 percent of the sample above the quantification  
13 limit. And the 1 percent -- 1 of the 28 is 4 percent.

14 Is that clear?

15 PANEL MEMBER BYUS: My question --

16 CHAIRPERSON FROINES: No, I don't want to -- no,  
17 my point is very simple.

18 PANEL MEMBER GLANTZ: I think the point they're  
19 trying to make here is that they found a lot of them.

20 CHAIRPERSON FROINES: What I want to say is a  
21 matter of presentation, not a matter of the content. What  
22 I want to see on a slide is what I'm going to be told in  
23 words. I don't want to have to do calculations. You're  
24 doing calculations in your head as you speak. And I don't  
25 want to do that. I want to see slides that reflect what

1 you're saying. And if you have to have five slides,  
2 that's fine. But it's -- I have no idea what has been  
3 said up to now on this issue, because I don't remember  
4 those numbers that you said. I can't.

5 Stan may, but that's another question.

6 So let's go ahead.

7 PANEL MEMBER BYUS: Just a minor question. I  
8 think the point is, what are you concluding by this slide?  
9 What's your conclusion? I mean you present this. Now,  
10 what's your conclusion? In one or two sentences, what is  
11 the conclusion of this what you just presented here?

12 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

13 FAN: Yeah, I just give the fact, what is from  
14 this application -- this monitoring the results is like  
15 that. That means that most of alpha-endosulfan we can --  
16 is volatilized as to the air, and the less  
17 beta-endosulfan, and in the application study. But in the  
18 ambient study we also get most of these alpha-endosulfan  
19 and much less in beta-endosulfan.

20 PANEL MEMBER BYUS: Okay. So that's your  
21 conclusion?

22 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

23 FAN: Yeah.

24 PANEL MEMBER BYUS: Okay.

25 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

1 FAN: But the concentration -- we don't have the  
2 concentration because Sheryl will talk about it. And we  
3 don't want to repeat, so we cut that off.

4 PANEL MEMBER BLANC: I think we should just move  
5 right into the next presentation. That would be awfully  
6 helpful to the --

7 DPR ASSOCIATE ENVIRONMENTAL RESEARCH SCIENTIST

8 FAN: It will be interesting.

9 DPR STAFF TOXICOLOGIST BEAUVAIS: Thank you.

10 PANEL MEMBER BLANC: You're welcome.

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

13 DPR STAFF TOXICOLOGIST BEAUVAIS: I'm Sheryl  
14 Beauvais from the Department of Pesticide Regulation, and  
15 I'll be talking about data and assumptions used to  
16 estimate exposures. And part of that will be a more  
17 detailed discussion of the studies that Dr. Fan was just  
18 talking about.

19 PANEL MEMBER LANDOLPH: Can I ask, which volume  
20 are you referring to now?

21 DPR STAFF TOXICOLOGIST BEAUVAIS: This is  
22 exposure assessment, which is volume 2.

23 PANEL MEMBER HAMMOND: Two.

24 DPR STAFF TOXICOLOGIST BEAUVAIS: Thank you.

25 Okay. Estimates were based monitoring done by

1 the Air Resources Board of endosulfan concentrations in  
2 air. Both ambient and application site monitoring was  
3 done using the sampling arrangements shown. And to start  
4 with I'll focus on the little sampler here.

5           This is the air sampling tube. It has two  
6 sections of sorbent, which was in this case XAD sorbent.  
7 This is the top end of the tube. This is the end that  
8 gets connected to the pump here. Tubes were connected to  
9 flowmeters and then on to the sampling pump here with  
10 Teflon tubing.

11           And during -- I want to highlight a couple of  
12 points during the methods validation portion when they  
13 were validating analytical methods. There were two pieces  
14 of information that I just want to pass along to you:

15           The first being that they did breakthrough  
16 testing, which is something you want to make sure  
17 basically that the sorbent that once it captures the  
18 analyte, the analyte stays there and doesn't simply pass  
19 through the tube and on out the pump. And in order to do  
20 that, what they do is spike the top end of the tube and  
21 run -- attach this to a sampler pump, in this case for 24  
22 hours at 2 liters per minute in the laboratory. And then  
23 at the end of that time analyze the two sections of  
24 sorbent separately. What you want to see is your analyte  
25 in the primary section and not in the back-up section.

1 And that's what was found here. There was no detectable  
2 amounts in the back-up section.

3 CHAIRPERSON FROINES: I have a question.

4 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

5 CHAIRPERSON FROINES: When we do air sampling,  
6 what we do, we use something called the Tisch sampler.  
7 And the Tisch sampler has a filter for collecting  
8 particulate. And it has a Tisch -- an XAD resin tube.  
9 And so we're collecting both particulate and vapors. And  
10 obviously the reason for that is -- I live in Los Angeles  
11 and we have lots of particulate. But unfortunately you  
12 guys live up in the area that now has heavy particulate as  
13 well.

14 And so the question is: Have you ever done any  
15 studies in which you've actually collected particulate and  
16 extracted things like endosulfan off the particulate?

17 DPR STAFF TOXICOLOGIST BEAUVAIS: I don't know.

18 CHAIRPERSON FROINES: Lyn?

19 DR. BEAUVAIS: The answer's no.

20 CHAIRPERSON FROINES: Why? With the levels of  
21 particulate that you have, you need to worry about  
22 adsorbed vapors.

23 ARB AIR POLLUTION SPECIALIST BAKER: Hi, Dr.  
24 Froines, members of the Panel. Lyn Baker with the Air  
25 Resources Board.

1           And we have in the past used a filter in front of  
2 the adsorbent resin when we were trying to differentiate  
3 the particulate phase from the gaseous phase of something.  
4 But then for an exposure assessment they've usually added  
5 it all together. So we typically have not been requested  
6 by DPR to differentiate. So we've usually just collected  
7 the -- with this type of an adsorbent tube, which is not  
8 obviously designed to collect particulate, but it will  
9 collect particulate, and we know that because the top of  
10 the adsorbent often is brown, where the adsorbent is  
11 white. So it's trapping some of the particulate.

12           CHAIRPERSON FROINES: Kathy.

13           PANEL MEMBER HAMMOND: There actually have been  
14 study looking at how well the adsorbent tubes -- this is  
15 Kathy Hammond, I'm sorry -- how well the adsorbent tubes  
16 collect particles. And there actually is a very high  
17 level of pass through, of the particles passing through  
18 the tubes. Intuitively you might think that particles are  
19 well adsorbed by the tubes or collected, but they're not.  
20 So, since even a volatile material -- you would have two  
21 things. You might have particles that contain endosulfan  
22 at the beginning and then you also might have vapor phase,  
23 endosulfan that condenses on to the surface of a particle.  
24 And those particles then could pass through this tube, and  
25 then you could underestimate exposure, which I think is

1 what Dr. Froines was talking about.

2 ARB AIR POLLUTION SPECIALIST BAKER: We certainly  
3 recognize there is some pass-through. But we know that  
4 the resin does trap some of the particles because we see a  
5 layer of particulate at the top of the bed of resin.

6 PANEL MEMBER HAMMOND: True. But you don't know  
7 what percentage that is.

8 ARB AIR POLLUTION SPECIALIST BAKER: Exactly.

9 PANEL MEMBER HAMMOND: In study -- I don't  
10 know -- for these materials I haven't done the studies.  
11 But for other studies, other kinds of tubes, charcoal  
12 tubes, which are similar designs, as much as 80 percent of  
13 the particles have been found to pass through, which I  
14 have to say I was surprised when I first saw it, those  
15 data.

16 CHAIRPERSON FROINES: I didn't want to hold it up  
17 any further. But I think this is an issue, Lyn, that we  
18 should come back to; and, that is, the generic issue of  
19 particles versus vapors. Because if you have an ultrafine  
20 particle with Telone on it, that's going to have a very  
21 powerful electrophilic effect in the lung. And since the  
22 ultrafines are absorbed into the cells, you're actually  
23 putting particles into the cells in the mitochondria and  
24 other places. And so this is an issue which hasn't been  
25 looked at to any degree. And I think it's an area of

1 pretty significant -- could have a significant impact.

2 PANEL MEMBER HAMMOND: May I, as long as you're  
3 on that part.

4 It also -- if the material itself is not very  
5 water -- not very soluble in the blood and not taken up  
6 quickly from the lung into the blood, if it's in the vapor  
7 phase it may be exhaled in a very high proportion; where  
8 if it's in the particulate phase, it might be trapped in  
9 the lung and therefore the dose -- the actual dose may be  
10 higher as well.

11 ARB AIR POLLUTION SPECIALIST BAKER: We'd  
12 certainly be happy to talk with you and DPR more about  
13 this.

14 CHAIRPERSON FROINES: Yeah. I mean your  
15 assumption that everything's going to get trapped on the  
16 XAD resin of course is the fundamental assumption. And  
17 it's just something that needs some experimental  
18 investigation, I think. It's not a fault. We're not  
19 under that.

20 So thank you.

21 DPR STAFF TOXICOLOGIST BEAUVAIS: But I can see  
22 that this is a source -- potential source of  
23 underestimation that will need to be mentioned in the  
24 exposure appraisal section of the document. So I'll add  
25 that in there.



1 from the end of July through the end of August. Sampling  
2 was conducted four days a week, and these were  
3 approximately 24-hour samples.

4 --o0o--

5 DPR STAFF TOXICOLOGIST BEAUVAIS: And to give you  
6 sort of a comparison here, this is the pesticide use  
7 report to summary of how much endosulfan was applied in  
8 Fresno County each month in 1996, in thousands of pounds  
9 here is what we're looking at here. And as you can see,  
10 we did -- the sampling did capture a high use period. But  
11 the high use actually occurred slightly before the  
12 sampling began in June and July.

13 Although we did -- we captured a high sampling  
14 period, it's questionable whether we captured the  
15 potentially highest concentrations. So that's a point  
16 that needs to be made.

17 --o0o--

18 DPR STAFF TOXICOLOGIST BEAUVAIS: And the sites  
19 for the air sampling, there were four sample sites. These  
20 were in Fresno County. Each of these was a sample mounted  
21 on top of the roof of a school. And then the background  
22 site was the ARB ambient air monitoring station in Fresno.  
23 This was an area where endosulfan use was not anticipated,  
24 and in fact the background samples collected at the site  
25 did not have endosulfan greater than the limit of

1 quantitation. It was below the LOQ for all samples for  
2 both alpha- and beta-endosulfan.

3 And the highest concentrations occurred at the  
4 San Joaquin Elementary School site.

5 --o0o--

6 DPR STAFF TOXICOLOGIST BEAUVAIS: Limit of  
7 detection. Just quickly acquaint you with this. The  
8 analytical limit of detection for alpha-endosulfan and  
9 beta-endosulfan are shown here. And then the limit of  
10 quantification in this case, to answer your question with  
11 numbers, in this case was 3.3 times the detection limit  
12 divided by the volume of air sampled.

13 So this is an analytical detection limit for the  
14 samples themselves, the resin. And then this is -- we get  
15 the LOQ. So the LOQ would depend on how long the sample  
16 was running. And this gives you a sense of what the LOQs  
17 are for the 24-hour samples.

18 And I'll point out here that endosulfan sulfate  
19 was analyzed, and all samples were below the LOQ. And so  
20 I'm not going to talk about that any further.

21 Endosulfan sulfate concentrations were not  
22 included in the total endosulfan. We looked only at the  
23 alpha- and beta-endosulfan in some of those to get total  
24 endosulfan concentrations for the exposure estimates.

25 PANEL MEMBER BYUS: And what was used for the

1 detection? What was the method?

2 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

3 WOFFORD: The analytical method?

4 PANEL MEMBER BYUS: Yeah, just -- what was it?

5 DPR STAFF TOXICOLOGIST BEAUVAIS: Electron  
6 capture detector. Unless you know that, my mind just went  
7 blank. It's in the document. I just went blank.

8 Sorry about that.

9 Okay. Quality assurance included collocated  
10 samples that will run each week; a trip blank, all of  
11 which were below the LOQ, which is what we want to see.  
12 And then now I need to talk about the spiked samples.

13 As I mentioned, we did have some recoveries that  
14 were very low. In the ambient air sampling, there were  
15 low recoveries in the field lab and trip spikes. These  
16 were all prepared at the same time at the start of the  
17 study and then stored until they were used. And all of  
18 them were, you know, 50 percent or lower and. The mean  
19 field spike recovery was 44 percent. It ranged between 38  
20 and 54 percent.

21 And -- yes.

22 PANEL MEMBER FRIEDMAN: What is a trip blank?

23 DPR STAFF TOXICOLOGIST BEAUVAIS: A trip blank  
24 goes along for the ride basically. It goes into the  
25 cooler where the samples are going to be put. And it

1 doesn't leave the cooler. So a field spike is one that  
2 goes and is hooked up to a pump. And in this case the  
3 field spikes during the ambient air monitoring were done  
4 in the Fresno -- or in the ambient air background site, a  
5 place where you don't anticipate endosulfan.

6 PANEL MEMBER GLANTZ: Now, when you say a field  
7 spike, does that mean you --

8 DPR STAFF TOXICOLOGIST BEAUVAIS: You spike it in  
9 the lab. You put a known amount of the endosulfan --  
10 alpha-endosulfan and the beta-endosulfan into endosulfan  
11 sulfates on each of the tubes and then see that you can  
12 recover the same amount when it comes back. So the spikes  
13 are analyzed along with the samples. And the trip blank  
14 is going along with it. It's looking for contamination in  
15 the handling process basically. So the trip blank is not  
16 connected to a pump, the field spikes are.

17 And so all of those were low. And then the lab  
18 spike is testing the analytical process, so it doesn't  
19 leave the lab. So in this case, the endosulfan  
20 recoveries -- alpha-endosulfan recoveries were all low.

21 But as you can see here, this is the mean  
22 alpha-endosulfan recovery and the beta-endosulfan recovery  
23 in the ambient air monitoring. And then for comparison  
24 I'm showing the application site means as well. And,  
25 again, the alpha-endosulfan was back up there again.

1           There was a quality assurance audit done of the  
2 procedures of all the study trying to detect what  
3 happened -- and trying to determine. And they came  
4 upon -- they didn't find any problems with their  
5 procedures or anything basically, but they determined that  
6 it was possible that what happened was that there was --  
7 the solutions were spiked with a commercially purchased --  
8 commercially purchased solutions of alpha- and  
9 beta-endosulfan. The manufacturer of the solutions  
10 recommended that they be stored at room temperature, and  
11 the laboratory stored them in the refrigerator. Now, what  
12 the laboratory procedures would have them do is warm them  
13 up to room temperature before use. But that -- and so  
14 that's a possibility. They essentially weren't able to  
15 determine exactly what the cause was there.

16           PANEL MEMBER HAMMOND: But did they spike the  
17 ambient and the application site samples at the same time?

18           DPR STAFF TOXICOLOGIST BEAUVAIS: No, these are  
19 two different times.

20           PANEL MEMBER HAMMOND: Was the same -- but --

21           DPR STAFF TOXICOLOGIST BEAUVAIS: They were  
22 started at two different times, in that ambient air  
23 monitoring was done in 1996 and application site monitor  
24 was done in 1997. And all samples were analyzed within 20  
25 days of collection. So, no, those are two different sets.

1 PANEL MEMBER HAMMOND: And do you know if the  
2 procedure for storing the standard was the same, or did  
3 they not refrigerate it in the second year?

4 DPR STAFF TOXICOLOGIST BEAUVAIS: That's a good  
5 question, and I can't answer that off the top of my head.

6 PANEL MEMBER HAMMOND: And it would certainly  
7 seem to me in -- if that happened in my lab, I would have  
8 done a little experiment to find out if refrigeration had  
9 that effect.

10 DPR STAFF TOXICOLOGIST BEAUVAIS: And they did.  
11 And I think they were getting equivocal results.

12 What?

13 Oh, here we go.

14 ARB AIR POLLUTION SPECIALIST BAKER: I'd just  
15 like to add, the analytical work and the spiking for these  
16 were actually done by two different labs, the Air  
17 Resources --

18 PANEL MEMBER HAMMOND: You mean for the ambient  
19 and application?

20 ARB AIR POLLUTION SPECIALIST BAKER: -- and  
21 application, yes.

22 Yes, the ambient was done by the Air Resources  
23 Board lab and -- the Air Resources Board staff did all the  
24 field sampling. But the Air Resources Board lab did the  
25 analysis for the ambient samples and the spiking. And so

1 it was our lab and our quality assurance audit of our lab  
2 that found this possible problem.

3 The Department of Food and Agriculture lab  
4 actually analyzed the samples for the application site  
5 monitoring a year later. And --

6 PANEL MEMBER HAMMOND: But ARB lab still spiked  
7 the samples?

8 ARB AIR POLLUTION SPECIALIST BAKER: No, the  
9 spikes were done I believe by the Department of Food and  
10 Agriculture lab.

11 So apparently it was something that our lab did  
12 inconsistent with the way they analyzed the samples when  
13 they actually spiked them. Because as the audit report  
14 for the study showed, the storage stability samples where  
15 you spike samples, put them in a freezer to make sure that  
16 you're not going to have degradation of the samples before  
17 you get them analyzed from the field, those results were  
18 all good. They were over 80 percent recoveries. So they  
19 apparently spiked the field samples differently than they  
20 spiked the storage stability samples.

21 So they have no reason to think that there was a  
22 problem with the actual ambient samples. They think the  
23 audit concluded that there must have just been a problem  
24 with the way they spiked the spiked samples for the  
25 ambient study.

1 PANEL MEMBER HAMMOND: I hear all that. I'm  
2 saying, if I thought that, then I would take the next step  
3 and just do a little experiment to see if that had an  
4 effect.

5 DPR STAFF TOXICOLOGIST BEAUVAIS: They did do a  
6 comparison.

7 PANEL MEMBER HAMMOND: Because one of the  
8 problems also, I understand it, is that in the recovery  
9 studies there's a very wide variation. It wasn't just  
10 that it was 44 plus or minus 2 percent, right? It was a  
11 huge variation in there. And that makes it very difficult  
12 to interpret the ambient air monitoring data.

13 DPR STAFF TOXICOLOGIST BEAUVAIS: True.

14 PANEL MEMBER HAMMOND: I mean I understand what  
15 you're saying and, you know, it may be okay, but we really  
16 don't know.

17 DPR STAFF TOXICOLOGIST BEAUVAIS: We don't know,  
18 that's true.

19 ARB AIR POLLUTION SPECIALIST BAKER: So Sheryl  
20 will explain the -- they accounted for our poor  
21 recoveries.

22 CHAIRPERSON FROINES: They what?

23 DPR STAFF TOXICOLOGIST BEAUVAIS: No, they didn't  
24 actually.

25 ARB AIR POLLUTION SPECIALIST BAKER: No, no, you.

1 You did.

2 DPR STAFF TOXICOLOGIST BEAUVAIS: Oh, I see what  
3 you're saying, what -- the next step, the procedure here.

4 What this slide is actually concluding is that we  
5 actually --

6 PANEL MEMBER HAMMOND: -- divided by .44?

7 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, we went  
8 ahead and corrected for these spike recoveries.

9 PANEL MEMBER HAMMOND: But you used .44?

10 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

11 PANEL MEMBER HAMMOND: But you did have some  
12 of -- some of your spiked samples have recoveries of 10  
13 percent, right?

14 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, and  
15 that's -- if we'd back up for a slide for a minute here.  
16 And I want to -- what we did was we corrected for mean  
17 field spike recovery, which had a range of 38 to 54  
18 percent. That's typical of what we would do. The labs --  
19 and, you know, and that's another thing that I don't know  
20 the answer to and, that is, whether lab spikes were done  
21 at -- were analyzed after or before --

22 PANEL MEMBER HAMMOND: I think that really levels  
23 the trip blank if I remember from document --

24 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay. Maybe it  
25 was the trip --

1           PANEL MEMBER HAMMOND: I think the lab was okay.  
2 I think it was -- it was either the field or the trip --  
3 the field and the trip were different from each other.

4           DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

5           PANEL MEMBER HAMMOND: And I forget which was the  
6 lower one. But --

7           DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, I'm --

8           PANEL MEMBER HAMMOND: But they didn't make sense  
9 anyway.

10          DPR STAFF TOXICOLOGIST BEAUVAIS: Okay.

11          PANEL MEMBER BYUS: So why did you choose 44  
12 percent and not the lowest recovery to be held protective?  
13 I mean that's just --

14          DPR STAFF TOXICOLOGIST BEAUVAIS: Well, to be  
15 health protective again, because the field spikes are the  
16 ones that went out in the field and were treated exactly  
17 the same as the samples. Those are the ones that --

18          PANEL MEMBER HAMMOND: Did you draw air through  
19 the field spikes?

20          DPR STAFF TOXICOLOGIST BEAUVAIS: Yes. Yeah,  
21 those --

22          PANEL MEMBER HAMMOND: So you do them for 24  
23 hours?

24          DPR STAFF TOXICOLOGIST BEAUVAIS: Yes. Yeah, the  
25 ambient air -- in this case for the ambient air study the

1 field spikes are done alongside the background sampling  
2 and --

3 PANEL MEMBER HAMMOND: Okay. Let me just  
4 postulate something.

5 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay.

6 PANEL MEMBER HAMMOND: I'll just -- you know, if  
7 we don't -- but I will postulate.

8 The trip blanks that had no air drawn through  
9 them had only 10 -- I think they had like 10 percent  
10 recovery.

11 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay.

12 PANEL MEMBER HAMMOND: The ambient air samples  
13 maybe also had 10 percent recovery. But because they were  
14 drawing air, you assume that air had no analyte there.  
15 But maybe it had analyte there and that's why it had a  
16 hard recovery.

17 DPR STAFF TOXICOLOGIST BEAUVAIS: No, they run  
18 concurrently with the background samples that had no --  
19 where the endosulfan was below the LOQ, which is what you  
20 want.

21 PANEL MEMBER HAMMOND: Which is in the same  
22 location?

23 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

24 PANEL MEMBER HAMMOND: They're collocated. Okay.

25 PANEL MEMBER BLANC: Yes. But you don't know

1 that the reason that the background samples were below the  
2 LOQ was because your recovery was so poor.

3 PANEL MEMBER HAMMOND: You get in a circle there.

4 DPR STAFF TOXICOLOGIST BEAUVAIS: Ah, I see what  
5 you're saying. You're right.

6 PANEL MEMBER HAMMOND: Yeah, it's just a circle.  
7 You just can't tell what you've got.

8 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes, you're  
9 right.

10 PANEL MEMBER HAMMOND: And also, it's not only  
11 that it's poor, but what makes it really even worse is  
12 that it's highly variable.

13 PANEL MEMBER BYUS: Right.

14 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay.

15 PANEL MEMBER BLANC: And just in your opinion,  
16 were these monitoring data to be submitted for  
17 publication, given what you're telling us about the  
18 variability of the adjustments that you made? Do you  
19 think it would be accepted for publication? Do you think  
20 peer-reviewed --

21 DPR STAFF TOXICOLOGIST BEAUVAIS: I have seen  
22 samples that go through contortions like this get  
23 published, yes.

24 (Laughter.)

25 DPR STAFF TOXICOLOGIST BEAUVAIS: And not

1 ideally, yeah.

2 Well, I think we can agree these data are less  
3 than ideal, yes.

4 PANEL MEMBER BLANC: And, Dr. Hammond, if you  
5 were reviewing this, you know, would you --

6 PANEL MEMBER HAMMOND: I would have difficulty --  
7 I'd have serious difficulty with knowing how to interpret  
8 the data. And I'd feel that it would be very, very  
9 difficult to have any understanding.

10 And I guess the other question I would have is --  
11 these things happen. I mean this happens, right? But  
12 then why was the ambient sampling not repeated?  
13 Especially since you're going back in the field to do  
14 application site sampling the following year, I would  
15 think then you would do ambient air monitoring again.

16 DPR STAFF TOXICOLOGIST BEAUVAIS: And I can't  
17 answer that question.

18 PANEL MEMBER HAMMOND: I mean it's probably --  
19 you know, it's probably ancient history now.

20 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

21 PANEL MEMBER HAMMOND: But it seems like --

22 DPR STAFF TOXICOLOGIST BEAUVAIS: Resource  
23 allocation, I don't know.

24 PANEL MEMBER HAMMOND: Yeah. And this may go  
25 back to Paul's earlier question about the number of

1 samples too.

2           And let me be clear. We know this isn't  
3 necessarily you personally, but we're just --

4           DPR STAFF TOXICOLOGIST BEAUVAIS: Sure.

5           PANEL MEMBER HAMMOND: But it seems like ambient  
6 air's an important measurement, important enough to decide  
7 to measure it. There were problems. It happens to me,  
8 you know. And those are the data that we say, "Okay, that  
9 was a pilot run and we have to figure out what went  
10 wrong," and then we repeat it. And this is -- to say the  
11 only data we have are data that are highly questionable is  
12 I think of concern, and I'm disappointed that that set of  
13 measurements wasn't repeated to understand.

14           CHAIRPERSON FROINES: Well, just -- I'd like to  
15 move on. But I think the Panel -- this Panel needs to  
16 think about this. Because, as we all know, endosulfan is  
17 a very, very dangerous pesticide. It's banned in most  
18 countries -- many countries throughout the world. And  
19 we're just talking about its regulation. So when we talk  
20 about health, we don't have any doubt that it's  
21 problematic from a TAC standpoint. So we need to decide  
22 what is -- what are we willing to accept in the exposure  
23 assessment so that we're comfortable with any  
24 determination we make.

25           DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, and

1 includes -- this is the application site data that I'm  
2 about to present under consideration. Because what  
3 happens to the monitoring adjacent to an application, the  
4 concentrations are higher, the risk numbers are -- of  
5 course it's much worse, you know, much lower MOEs for the  
6 application site monitoring for the bystander exposures.  
7 And any mitigation measures that we take to cover  
8 them -- to bring down bystander exposure would then  
9 involve a lessening of the ambient air as well.

10 PANEL MEMBER HAMMOND: Except for the  
11 volatilization that was mentioned earlier that might  
12 happen over the next several days afterwards.

13 CHAIRPERSON FROINES: And that might  
14 underestimate it.

15 PANEL MEMBER BYUS: And it won't affect it at  
16 all.

17 CHAIRPERSON FROINES: That would underestimate  
18 it.

19 PANEL MEMBER BYUS: Theoretically --

20 DPR STAFF TOXICOLOGIST BEAUVAIS: Well, because  
21 it would involve decreased application rates, for example,  
22 decreased numbers of applications that are allow, the  
23 source of things that --

24 PANEL MEMBER HAMMOND: Well, that kind of --

25 DPR STAFF TOXICOLOGIST BEAUVAIS: That kind of

1 mitigation measure, yeah. Yeah, I'm sorry. I'm speaking  
2 regular --

3 PANEL MEMBER BYUS: But 50 to 70 percent of what  
4 you spray under ideal conditions revolatilizes, is going  
5 to contribute to the ambient air. Nothing you can do  
6 other than reducing the amount of total exposure is going  
7 to affect that. Am I wrong on that?

8 PANEL MEMBER HAMMOND: It reduces total  
9 application?

10 PANEL MEMBER BYUS: Huh?

11 PANEL MEMBER HAMMOND: Reduced total application.

12 PANEL MEMBER BYUS: Reduced total application.  
13 So nothing other than reduced total application is going  
14 to reduce theoretically, since you have such a high  
15 percentage of it that goes into the air and then it has  
16 such a long half-life. So really nothing you're going to  
17 mitigate other than reducing the total amount that you  
18 spray is going to really affect that. And then of course  
19 but then your ambient air data is kind of weak, so -- or  
20 nonexistent. But that's okay.

21 I just want to make sure I have it clear in my  
22 mind.

23 CHAIRPERSON FROINES: Let's go ahead, because we  
24 are going to have to deal with the issue of the MOE, and  
25 the MOE depends upon what we're going through right now.

1 So let's --

2 PANEL MEMBER HAMMOND: What the E is.

3 CHAIRPERSON FROINES: What?

4 PANEL MEMBER HAMMOND: It depends on E. MOE  
5 depends on E.

6 DPR STAFF TOXICOLOGIST BEAUVAIS: Exposure.

7 (Laughter.)

8 CHAIRPERSON FROINES: I can't keep up.

9 (Laughter.)

10 CHAIRPERSON FROINES: Let's go ahead.

11 But I'm just putting those words out so people  
12 are thinking about them as we go forward.

13 DPR STAFF TOXICOLOGIST BEAUVAIS: Next slide.

14 --o0o--

15 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay. These  
16 are the ambient air concentrations. And this is -- each  
17 of these are the sites. And this is the San Joaquin  
18 County Elementary School site.

19 On the Y axis, this is a mean concentration or  
20 the concentration of micrograms per cubic meter. Each bar  
21 is -- this is -- the blue bars are alpha-endosulfan and  
22 the red bars are beta-endosulfan. Arrow bars are standard  
23 deviation.

24 So to get the concentration used in the exposure  
25 estimate from this, I took the mean alpha-endosulfan and

1 added it to the mean beta-endosulfan. So mean total is  
2 .062 micrograms per cubic meter. So you'll see this again  
3 momentarily when I'm talking about exposure estimates.

4 And in calculating the mean and standard  
5 deviation for any samples that were below the LOQ, I used  
6 half the LOQ.

7 So, again, when we're talking about that gray  
8 area between detection and quantification, take half the  
9 LOQ assigned to that or substituted for that.

10 PANEL MEMBER BLANC: And can you tell me what the  
11 median values were?

12 DPR STAFF TOXICOLOGIST BEAUVAIS: Off the top of  
13 my head, no. But --

14 PANEL MEMBER BLANC: Was it skewed to the right?

15 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

16 PANEL MEMBER BLANC: So it was skewed towards  
17 higher concen -- skewed this way, right?

18 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes, exactly.  
19 There's a long tail on -- a lot of non-detects.

20 PANEL MEMBER BLANC: Oh, so it's skewed  
21 towards --

22 DPR STAFF TOXICOLOGIST BEAUVAIS: A low LOQ,  
23 yeah.

24 PANEL MEMBER HAMMOND: No, that makes it high  
25 here and it stems out. So you're still --

1 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, what  
2 you're saying is correct. Yes, it is skewed.

3 PANEL MEMBER BLANC: I mean was the median higher  
4 than the mean? Maybe I should be asking it that way.

5 DPR STAFF TOXICOLOGIST BEAUVAIS: I wouldn't --  
6 no, I wouldn't think so. It should be lower.

7 PANEL MEMBER BLANC: Okay.

8 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah,  
9 because --

10 PANEL MEMBER HAMMOND: It usually is --

11 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, it would  
12 be lower. The median is going to be the center --

13 PANEL MEMBER BLANC: Right. And --

14 PANEL MEMBER HAMMOND: The median could have been  
15 less than detectable.

16 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, exactly.

17 PANEL MEMBER HAMMOND: I don't know the lots, but  
18 it could have been.

19 PANEL MEMBER BLANC: No, because we had the  
20 numbers -- most of them were detectable at least for  
21 the --

22 PANEL MEMBER HAMMOND: Right. Well, I don't  
23 know, do we -- were those percentages from the previous  
24 speaker's slides the percentages for these samples?

25 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, for the

1 part that she talked about for the ambient air, which was  
2 just the bottom half of her slide.

3 PANEL MEMBER HAMMOND: So something like 96  
4 percent were detectable, do you think?

5 DPR STAFF TOXICOLOGIST BEAUVAIS: No, that's the  
6 application site that that's true of.

7 PANEL MEMBER HAMMOND: Oh, okay. But it's 8 -- I  
8 think it's still pretty high.

9 OEHTA AIR TOXICOLOGY AND EPIDEMIOLOGY

10 BRANCH CHIEF MARTY: 88 percent for alpha.

11 PANEL MEMBER HAMMOND: 88 percent?

12 Yeah, 88 percent are greater than LOQ for alpha.

13 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

14 PANEL MEMBER HAMMOND: So these are exactly the  
15 same data as these that you're talking about?

16 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes, this is  
17 the same data, yes.

18 PANEL MEMBER HAMMOND: So these are 75 ambient  
19 samples, is that right?

20 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

21 PANEL MEMBER HAMMOND: This is 75?

22 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, the N on  
23 each of those bars is 18 or 19 samples. So 18 or 19  
24 samples per site.

25 PANEL MEMBER HAMMOND: So these are mostly

1 detectable, unquantifiable?

2 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

3 PANEL MEMBER BLANC: I guess my question is  
4 related to -- since so much of the -- leaving aside all of  
5 the other error factors, these mean values are going to be  
6 driving a lot of your future calculations?

7 DPR STAFF TOXICOLOGIST BEAUVAIS: For the ambient  
8 air it does, yes.

9 PANEL MEMBER BLANC: So is -- maybe, Kathy, you'd  
10 want to comment on this. Is the mean the most  
11 conservative public health protective metric to use, or  
12 should it be the 75th percentile?

13 PANEL MEMBER HAMMOND: Compared to the median,  
14 yes.

15 PANEL MEMBER BLANC: And what about compared to  
16 the 75th percentile?

17 PANEL MEMBER HAMMOND: Well, I mean I think what  
18 I -- I was going to wait till I got to hear what's being  
19 said, to give her a chance to give the talk.

20 But I mean I think one of the things to talk  
21 about from what I read here is this 95 percent value  
22 that's in there. I mean all of these are going to have to  
23 be looked at --

24 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay.

25 PANEL MEMBER HAMMOND: -- and how they're used.

1 But I think one -- the mean is -- if you want to know what  
2 the mean, you know, exposure is. But if you want to take  
3 a look at what's the public health protective, you have to  
4 go to something higher, like a 95th percentile, or even  
5 a -- and I actually think that maximum concentrations  
6 should be reported. That was one of the questions, is  
7 that are your whiskers there, are those to the maximums?  
8 Sometimes those are like times so many standard deviations  
9 or inter-quartile. Actually it turns back -- because you  
10 don't standard definitions.

11 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, the air  
12 bars in this case are standard deviations. So --

13 PANEL MEMBER HAMMOND: So that's only the  
14 standard deviation?

15 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

16 PANEL MEMBER HAMMOND: Oh, oh. Then do you have  
17 the maximum value for those samples?

18 DPR STAFF TOXICOLOGIST BEAUVAIS: I can tell you.  
19 I think it was the point --

20 PANEL MEMBER GLANTZ: Yeah. Boy, I'll tell you  
21 if those are standard deviations, then they're very skewed  
22 as to --

23 DPR STAFF TOXICOLOGIST BEAUVAIS: And actually  
24 what I would like to do to -- before we spend a lot of  
25 time on this --

1           PANEL MEMBER GLANTZ:  If those are the standard  
2  deviations, they're very skewed distributions, and it  
3  doesn't really even make sense to talk about the mean.  
4  You really ought to be presenting this as --

5           PANEL MEMBER HAMMOND:  Well, you know, let me  
6  just say -- and I'm sorry that we're kind of jumping  
7  around a lot while giving your presentation -- as long as  
8  we're saying this, I would expect it to be extremely  
9  skewed.  There's certain tables in here that surprised me  
10 because the standard deviation is equal to the mean, and  
11 that to me is too small.  I would expect it to be higher  
12 in this kind of -- these kind a data, because we're  
13 talking here -- you say, well, four days a week for the  
14 entire month of August, right? -- Monday through Thursday  
15 the entire month.  And I think you do not have the data,  
16 if I understand from this -- or maybe you do -- as to  
17 whether or not any endosulfan was actually being applied  
18 during that time, I mean to the days you can't associate  
19 the sample --

20           DPR STAFF TOXICOLOGIST BEAUVAIS:  We cannot, no.

21           PANEL MEMBER HAMMOND:  -- that's sprayed in it?

22           DPR STAFF TOXICOLOGIST BEAUVAIS:  No, because the  
23 use report data are only reported to within a square mile.

24           PANEL MEMBER HAMMOND:  I understand that.  But I  
25 mean you don't even know if they were applied that day --

1 day by day, do you?

2 Was any applied in the entire county or in that  
3 square mile --

4 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes, there was.

5 PANEL MEMBER HAMMOND: You do have that  
6 information?

7 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes, I do.

8 PANEL MEMBER HAMMOND: Because I think that  
9 that's another way that these data need to be looked at.  
10 But, you know, certainly there were days in which there  
11 was no application, right, in which you have sampling. So  
12 that's going to give you -- you know, stand the, you know,  
13 real low values. And then you're going to have days the  
14 application might have been very nearby.

15 So I would expect if you had 10,000 samples  
16 collected in Fresno, you would have a very wide range, you  
17 know, highly dispersed data.

18 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

19 PANEL MEMBER HAMMOND: I mean that's what one  
20 would expect here.

21 CHAIRPERSON FROINES: Keep in mind, Kathy, one  
22 thing, that they are using one half of the LOQ for  
23 their --

24 PANEL MEMBER HAMMOND: I understand. But they  
25 only have 12 percent of the samples that are -- for which

1 that's true. So that's not affecting much. It has  
2 very --

3 CHAIRPERSON FROINES: It's not affecting much.  
4 But it's different than calling it zero or ignoring --

5 PANEL MEMBER HAMMOND: But it really has no  
6 effect on the data here. If they then made it zero, it  
7 wouldn't change really, because -- but if -- so you do  
8 have a -- you started to look up, before we kind of truck  
9 you in 14 different directions, the maximum values.

10 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah. And  
11 it's -- I've got a good size table here and so I can tell  
12 you this in a little bit. But --

13 PANEL MEMBER HAMMOND: Or maybe you can do that  
14 later --

15 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

16 PANEL MEMBER HAMMOND: -- after a break or  
17 something. Maybe you need to get through your talk or  
18 something. But I do think that understanding what the  
19 maximum values are --

20 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay. Yeah,  
21 I'm seeing values here around .3 -- .31, .28. And so we  
22 know that they go at least that high. And I think that  
23 might be the highest.

24 PANEL MEMBER HAMMOND: .3, .38?

25 DPR STAFF TOXICOLOGIST BEAUVAIS: .28, .31.

1 CHAIRPERSON FROINES: Gary, did you --

2 PANEL MEMBER FRIEDMAN: I was just thinking --  
3 maybe you're going to get to this.

4 PANEL MEMBER HAMMOND: Yeah, I am.

5 PANEL MEMBER FRIEDMAN: But do you know the  
6 days that --

7 DPR STAFF TOXICOLOGIST BEAUVAIS: Probably --  
8 hey, if we let you.

9 PANEL MEMBER FRIEDMAN: If you know the days that  
10 they're spraying, maybe, you know, if you look at that day  
11 and the next day, get at the question of volatile -- you  
12 know, spread a volatile material versus the drift issue.

13 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay. And I  
14 have not done this specifically with endosulfan. I did  
15 this with the last compound I came before this panel with,  
16 which was Methidathion. And you have -- it's difficult to  
17 interpret because you have, you know, maybe two or three  
18 applications that happened a day or two before the  
19 monitoring started and it's difficult to determine how far  
20 away you should go from the sections -- the  
21 one-square-mile sections. I mean within the county  
22 certainly there's applications on a daily basis. Fresno  
23 County in 1996 was using a lot of endosulfan.

24 So the question is: How close do I need to get?  
25 And then how many days before and after? And within

1 those -- so I can certainly do that work. But I guess to  
2 also clarify that we -- when we look at this from a  
3 regulatory standpoint, we're focusing -- the worst case  
4 scenario for ambient air is for the person who's adjacent  
5 to an application. And so that's where we're using the  
6 upper bound estimate from the application site monitoring  
7 to cover that. And then these -- we have seasonal  
8 estimates for application site as well as for ambient air.

9 CHAIRPERSON FROINES: Let's go ahead.

10 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay.

11 --o0o--

12 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay. Now I'm  
13 going to talk about application site monitoring. This  
14 occurred in 1997. And ARB monitored an application of  
15 endosulfan to an apple orchard. And the applied rate was  
16 1.5 pounds of endosulfan to acre -- per acre. And the  
17 maximum allowed on apples is 2.5. So for the short-term  
18 exposure estimate for that acute I accounted for that  
19 difference. And I'll be talking about that in a minute.

20 --o0o--

21 DPR STAFF TOXICOLOGIST BEAUVAIS: There were --  
22 in this application site study there were four sampling  
23 stations that surrounded the orchard. The wind direction  
24 was from the west during the application and for several  
25 hours afterwards. And so this east sampling site had the

1 highest concentrations of endosulfan.

2 --o0o--

3 DPR STAFF TOXICOLOGIST BEAUVAIS: And this is  
4 showing the samples. Sample No. 1 is the application.  
5 And then these are the post-application samples. And  
6 earlier when Pam was saying that the highest endosulfan  
7 concentrations occurred after the application, that will  
8 be the next graph that I show you here in a minute. But  
9 I'm just going to let you know -- just sort of orient you  
10 as to what these sample intervals are. There were a total  
11 of seven. The first five covered the first day  
12 essentially. It's 26.75 hours by the time you total all  
13 these hours.

14 And as you can see, the wind was directly out of  
15 the west during the early part where these highest  
16 concentrations were happening.

17 And then we have -- after that first day we have  
18 sample 6 and 7, each of which was a 24-hour sample. So we  
19 had a total of three days.

20 So I have a 24-hour time-weighted average that  
21 covers this first 26.75 hours. That's samples 1 through  
22 5. And then a three-day time-weighted average that I'll  
23 be talking about for the seasonal and annual exposure  
24 estimates that incorporated these last two as well.

25 --o0o--

1 DPR STAFF TOXICOLOGIST BEAUVAIS: And analytical  
2 detection limits were similar in this study to the  
3 previous one. And again all samples were below the LOQ  
4 for endosulfan sulfate, so only alpha-and beta-endosulfan  
5 were included in the total endosulfan estimates. Total  
6 endosulfan concentrations used estimate exposure. Again,  
7 we had duplicate collocated samples. And background and  
8 trip blanks were all below the LOQ.

9 In this case we had acceptable recoveries for the  
10 field lab and trip spikes. Alpha-endosulfan mean recovery  
11 of the field spikes was 85 percent. The range of all  
12 recoveries was 78 to 90. And the range was 57 to 66. So  
13 we had a lower recovery for beta-endosulfan in this study.

14 --oOo--

15 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay. And this  
16 is a summary graph of the application site concentrations,  
17 where each of these sets of bars is a sample -- represents  
18 a sample interval. Concentrations are given in micrograms  
19 per cubic meter. And each of these bars is the total  
20 alpha plus beta endosulfan, with the red bars being from  
21 the -- this east sampling site. The little bars on the  
22 left are from the north, and yellow and the dark -- black  
23 I guess are from the south and west respectively.

24 So, again, the east's sampling station had the  
25 highest endosulfan concentrations. And to determine the

1 24-hour total endosulfan that we used for short-terms  
2 exposure estimate, just multiply the concentration of each  
3 interval at that east station times the time and then  
4 divide by the total time.

5           And so you get the -- this 24-hour time-weighted  
6 average was 1.63 micrograms per cubic meter, and then it  
7 was adjusted for the fact that this wasn't a maximum  
8 allowed application rate. So it was multiplied by that  
9 1.67 the ratio of 2.5 to 1.5 pounds they had per acre. So  
10 this is the concentration that is used in the short-term  
11 exposure estimates.

12           And then for long-term concentration, which is  
13 going to be the three-day time-weighted average I used to  
14 calculate seasonal and annual exposures, this is all  
15 the -- average calculated like that for all seven samples.

16           PANEL MEMBER HAMMOND: I think this is very  
17 interesting. But I'm looking at -- you know, I just  
18 quickly looked up. So your three is -- the top bar there  
19 is the two to six hours after application.

20           DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah. That's a  
21 four-hour sample, yeah.

22           PANEL MEMBER HAMMOND: So we're seeing quite a  
23 bit after application; one is during the application?

24           DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

25           PANEL MEMBER HAMMOND: And then sample 4 is 6 to

1 14 hours, you know, which -- I'm trying to see this one  
2 panel. But number 6 is your 24 to 48 hours. And number 7  
3 is your 48 to 72 hours. And what I noticed there is that  
4 those two numbers aren't changing.

5 So, if you had to guess what 72 to 96 hours was.

6 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

7 PANEL MEMBER HAMMOND: So we -- you know,  
8 everything you have there is correct. But if we were to  
9 think about what's the long-term exposure, not a  
10 three-days but if we were to say two weeks, it might be  
11 that it might actually be continuing, that may be a very  
12 slow --

13 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah. And  
14 actually for my long-term calculations I'm using a month  
15 for that.

16 PANEL MEMBER HAMMOND: And you keep it at level  
17 7?

18 DPR STAFF TOXICOLOGIST BEAUVAIS: I use that  
19 three-day time-weighted average and multiply that by a  
20 month.

21 PANEL MEMBER HAMMOND: Oh, I see. You say that's  
22 the level of those for a month.

23 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

24 PANEL MEMBER HAMMOND: Now, the other thing  
25 that's happening is presumably there are other fields

1 being sprayed.

2 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, right.

3 PANEL MEMBER HAMMOND: And so that's the other  
4 part that goes into that assumption?

5 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

6 And the background -- now, there was background  
7 sampling done, the pre-application samples, and no  
8 alpha-endosulfan -- I'm sorry -- no endosulfan. All the  
9 pre-application samples were below the LOQ.

10 PANEL MEMBER HAMMOND: And so there were not --  
11 no other fields just had -- you were talking earlier about  
12 there might have been other fields that have been sprayed  
13 or had applications and --

14 DPR STAFF TOXICOLOGIST BEAUVAIS: Well, I can't  
15 address whether or not there was a field, for example, on  
16 day two during this sample interval 6. There could have  
17 been a field somewhere around there that was being  
18 sprayed. I don't know. We only --

19 PANEL MEMBER HAMMOND: But it is interesting that  
20 there was nothing at all beforehand.

21 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah. They  
22 were below the LOQ, yeah.

23 PANEL MEMBER HAMMOND: That's very interesting.

24 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

25 --o0o--

1           DPR STAFF TOXICOLOGIST BEAUVAIS: Okay. Those  
2 are the data that are used to calculate exposure. And to  
3 calculate exposure, we would estimate absorbed dose for  
4 the bystander and ambient air estimates as a total, alpha  
5 plus beta endosulfan. Assume a hundred percent of the  
6 inhaled pesticide is absorbed. And so it's simply air  
7 concentration times the inhalation rate for adults. And  
8 infants we use slightly different inhalation rates. And  
9 these are the ones that we typically use in calculating  
10 exposures.

11           The air concentrations again. For ambient air we  
12 use the data from the highest sampling station, which was  
13 the San Joaquin Elementary School. And for bystanders,  
14 that east station application monitoring.

15           And then also, we don't know -- people could be  
16 potentially exposed to endosulfan every day of the year.  
17 You know, that's sort of like the background assumption.  
18 We really don't know what individual exposure patterns  
19 are. What we do is we take the use data and we make an  
20 assumption here that exposures are less likely to occur  
21 during months when there's very little use. And in this  
22 case we use an arbitrary cutoff of 5 percent of the annual  
23 total that was used during that month.

24           So we don't have great resolution. And so we  
25 just simply take a monthly total here. And this -- so

1 what you're looking at here is a graph that's a five-year  
2 average between -- in this case, between the years 2000  
3 and 2004 of how much endosulfan was applied in Fresno  
4 County each month by all methods on all crops. And then  
5 the question is: How much of it was applied in February  
6 and March and so forth. And what we find here is that  
7 that 5 percent cutoff, seven of these months are above  
8 that. And so we say that the exposure's most likely to  
9 occur during those seven months. And so that's when we  
10 annualize. We say that seven months is the 7 out of 12.  
11 And I'll show you here in the calculations.

12 --o0o--

13 DPR STAFF TOXICOLOGIST BEAUVAIS: For the  
14 seasonal -- we do both seasonal and annual. And I'm not  
15 doing a short-term ambient air concentration because I'm  
16 using the bystander -- the application site data to cover  
17 for that. So we're assuming that that's the worst case  
18 for an ambient air, is somebody who's adjacent to  
19 applications.

20 And so for the seasonal it's just simply the  
21 concentration times the inhalation rate.

22 And then the annual, we annualize it by saying  
23 that, well, they have these high use months. So 7 divided  
24 by 12 in this case here. And so this the concentration.  
25 This mean concentration from the San Joaquin Elementary

1 School site times the inhalation rate times that 7 over  
2 12. And so this is how the annual average daily dosage is  
3 calculated.

4 And the next slide.

5 --o0o--

6 DPR STAFF TOXICOLOGIST BEAUVAIS: And bystander  
7 calculations. Now we have a short term that's also going  
8 to cover the ambient air exposure. And here we have this  
9 short-term concentration, which was the 24-hour  
10 time-weighted average that was adjusted again upwards for  
11 the application rate. And so the short term is simply  
12 this concentration times the inhalation rate, which is  
13 higher in infants than adults.

14 Season and annual average daily dosages were  
15 calculated in the same way as for ambient, except that we  
16 were looking at the pesticide use report data at how many  
17 applications are made. We don't know where the sites are  
18 located, but they give us site identifiers, field  
19 locaters. And so from that we're seeing that you don't  
20 see the same one popping up over and over again over a  
21 period of months.

22 And in most cases there's a limitation as to how  
23 often you can apply endosulfan per year. In fact, I think  
24 it's all but tomatoes you have like at most one or two  
25 applications I think that is -- that are allowed.

1           So for the bystander exposures we're assuming one  
2 month rather than seven months, because the person --  
3 there is no evidence to suggest that there be multiple  
4 locations or multiple uses at a location over a  
5 seven-month period.

6                               --o0o--

7           DPR STAFF TOXICOLOGIST BEAUVAIS: And these are  
8 the exposure estimates. So for the short-term exposures,  
9 again for the ambient air we're taking the bystander  
10 estimates to cover those and then seasonal and annual  
11 exposure estimates.

12           Next slide.

13                               --o0o--

14           DPR STAFF TOXICOLOGIST BEAUVAIS: So to talk  
15 about some of the uncertainties, which we have been  
16 talking about, the recoveries for the alpha-endosulfan  
17 during -- spikes during the ambient air sampling were low.  
18 And so to -- and they were unable to confirm the reason in  
19 the quality assurance audit -- determined that it possibly  
20 had to do with the refrigeration of the spiking solutions.

21           But we did the -- we corrected for the field  
22 spike recoveries. And this is the effect that you get on  
23 the concentrations. These are the uncorrected and then  
24 the corrected for field spike recoveries.

25           So this is just a graph that you've already seen.

1 And this is what it would look like without the  
2 correction.

3 --o0o--

4 DPR STAFF TOXICOLOGIST BEAUVAIS: And, finally,  
5 ambient air. Now, as we -- a couple things that I need to  
6 say on this slide. The first piece is what's already up  
7 there, which is that the ambient air exposure estimates  
8 could have been overestimated, because again, as we've  
9 seen earlier, use has been decreasing annually since the  
10 monitoring was done in 1996.

11 However, as I showed on the earlier slide, we  
12 didn't necessarily capture the highest use period. And so  
13 there's possibility that it was underestimated. And there  
14 may be other reasons as well.

15 And I have some other things here that I  
16 obviously need to talk about now in the appraisal.

17 And that is it. Do you have any other questions?

18 PANEL MEMBER BYUS: Just one quick question. I  
19 mean you showed the picture of the airplane spraying  
20 versus that thing.

21 Do airplanes spray endosulfan?

22 DPR STAFF TOXICOLOGIST BEAUVAIS: Sure. There  
23 are applications, yes.

24 PANEL MEMBER BYUS: Do you have some feeling  
25 about drift compared to airplanes versus whatever that is?

1 DPR STAFF TOXICOLOGIST BEAUVAIS: No, that's an  
2 air blast that you're looking at there.

3 PANEL MEMBER BYUS: Air blast. What's your --

4 DPR STAFF TOXICOLOGIST BEAUVAIS: This is what  
5 you would see in an orchard application. So this is the  
6 type of application that was monitored.

7 There are some studies where they have looked at  
8 both air and ground methods. And air blast is in those  
9 studies. And this isn't endosulfan. This is other active  
10 ingredients. But it's in the general range of the aerial.  
11 Sometimes it's higher, sometimes it's slightly lower.

12 And then when you talk about the ground being  
13 sprayed with methods where they're -- you've got the boom  
14 that's pointed downwards. In this case you've got a spray  
15 that's going upwards. And it's with air jets that are  
16 basically trying to deposit it all over these leaves and  
17 move the leaves around. So you've got quite a cloud going  
18 into the air there.

19 But when you've got the spray boom where the  
20 spray's pointed downwards and you're trying to minimize  
21 this off-site with the sort of management methods we we're  
22 talking about earlier, those off-site concentrations are  
23 lower. So --

24 PANEL MEMBER BYUS: So this is kind of more of  
25 the -- it's I mean the maximal dispersion and drift,

1 whatever?

2 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, for  
3 ground methods this would be the worst, yeah.

4 PANEL MEMBER BYUS: What'd be their worst case  
5 scenario of an application? That's my question.

6 DPR STAFF TOXICOLOGIST BEAUVAIS: Pretty close,  
7 yeah.

8 PANEL MEMBER LANDOLPH: In that air blast is he  
9 wearing -- the person spraying it, are they wearing  
10 respirators? And do they ever get sick? Any toxicity  
11 symptoms from spraying this stuff?

12 DPR STAFF TOXICOLOGIST BEAUVAIS: They  
13 can -- now, in this case I think this individual's in an  
14 enclosed cab. If they're not, they're wearing a  
15 respirator.

16 PANEL MEMBER HAMMOND: It seems to me -- this is  
17 a question -- going back to Craig's question.

18 In the text -- I'm not going to be able to find  
19 it now -- but I think I remember seeing and being  
20 surprised to see that the flaggers had lower exposures --  
21 these were personal samples on the -- occupational  
22 exposures -- that the flaggers had lower exposures than  
23 the pilots of the planes. And I was always traditionally  
24 taught that they would -- the flaggers would have much  
25 higher exposures except for when the planes crashed --

1 (Laughter.)

2 PANEL MEMBER HAMMOND: -- which happens, and it's  
3 more frequently than one would expect.

4 DPR STAFF TOXICOLOGIST BEAUVAIS: Now, the  
5 flagger data set that we have access to is a fairly small  
6 data set. And so it may be an artifact of that small  
7 monitoring data set.

8 PANEL MEMBER HAMMOND: Okay. Because that was  
9 like a very surprising kind of finding. Because usually  
10 it's like much higher because they're on the ground  
11 getting sprayed. And it makes you -- and if you're in the  
12 plane, you're not getting. Going back over your path,  
13 but --

14 DPR STAFF TOXICOLOGIST BEAUVAIS: Well, in this  
15 case I'm also assuming an open cockpit plane. I'm not  
16 assuming an enclosed cockpit at all.

17 PANEL MEMBER HAMMOND: So --

18 DPR STAFF TOXICOLOGIST BEAUVAIS: So this is  
19 someone that could conceivably turn around and drive right  
20 back through their own swath.

21 PANEL MEMBER HAMMOND: So you basically were  
22 working from the means of your values when you did all  
23 these calculations?

24 DPR STAFF TOXICOLOGIST BEAUVAIS: What we do for  
25 short-term exposures, we try to come up with an upper

1 bound estimate. And that's where that 95th percentile  
2 comes in.

3 PANEL MEMBER HAMMOND: So that was a question I  
4 had. Was that an observed 95th percentile or the  
5 calculated estimate of the 95th percentile value? Or was  
6 that the 95th percent -- upper confidence limit for the  
7 mean value?

8 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay. No,  
9 it's -- what that is is that is an upper bound -- it's a  
10 95th percentile using log normal methods, if I remember  
11 right. I'll have to check that for these. But that's --  
12 but that is of the data set.

13 PANEL MEMBER HAMMOND: It's trying to estimate --

14 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

15 PANEL MEMBER HAMMOND: -- the 95th percentile  
16 statistically from the data?

17 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

18 PANEL MEMBER HAMMOND: Okay. That's what you're  
19 trying to do?

20 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

21 PANEL MEMBER HAMMOND: Okay. And those were the  
22 numbers that you used to do all these calculations?

23 DPR STAFF TOXICOLOGIST BEAUVAIS: For the short  
24 term. And then for long term -- basically what we're  
25 trying to do for the short-term exposures, we're trying to

1 get a reasonable worst-case estimate. For long-term  
2 exposures we're assuming that not every exposure's the  
3 maximum. And when you look at the pesticide use report  
4 data you find that, that a lot of times they're applying  
5 it half the maximum allowed application rate or sometimes  
6 less. So we're going for more of a typical exposure for  
7 the long-term estimates.

8 PANEL MEMBER HAMMOND: Using the mean?

9 DPR STAFF TOXICOLOGIST BEAUVAIS: And that's  
10 where we're using the means, yes.

11 PANEL MEMBER HAMMOND: So let me go back to the  
12 bystander for just a minute just to keep -- before we get  
13 too confused.

14 DPR STAFF TOXICOLOGIST BEAUVAIS: Sure.

15 PANEL MEMBER BYUS: Saying that at the bystander  
16 where you've got your estimate of 95th percentile, did you  
17 ever go back and look at your maximum measured value to  
18 see how that related to your estimated 95th percentile  
19 value? Because one of the things -- I mean I think it's  
20 worthwhile trying to do. And the reasons given in the  
21 report, and they do make sense, are the -- with the small  
22 number of samples, it's hard to know where your 95th  
23 percentile value is. You're probably better calculating  
24 it. And the reality is if you do a lot of looking at  
25 exposure data, especially when it's so skewed, as these

1 data would be and would be expected to be, that it's very  
2 unlikely, very unlikely that if you do a hundred samples,  
3 which is more than what was done here, if you collect a  
4 hundred samples you're unlikely to actually get things in  
5 the upper 5 percentile. Even though you might think you  
6 would, you're actually unlikely --

7 DPR STAFF TOXICOLOGIST BEAUVAIS: So your upper  
8 bound estimate is oftentimes above --

9 PANEL MEMBER HAMMOND: Right. You're actually  
10 underestimating the upper bounds if you do it from  
11 sampling data directly. But it's also, I always think,  
12 still useful to look at your data. But, you know, it's  
13 specifically to look at those maximum values and see.

14 But it's very difficult to actually capture the  
15 true maximum values. But at least look at the maximum to  
16 see, because you might for some reasons have missed some  
17 behavior or something that's happening that can lead to  
18 those higher values.

19 And certainly when one's looking at chronic  
20 effects, which I assume is what you're -- when you're  
21 doing your annual levels, you're talking about chronic  
22 effects -- then mean values are the -- what you want to  
23 know are people's mean exposures through the year and  
24 using an arithmetic mean as the appropriate...

25 PANEL MEMBER LANDOLPH: Okay. I've just got a

1 quick question.

2           On page 11 under "Reported Illnesses," which is a  
3 very interesting section, I noticed there are a couple  
4 sections in volume 2 where you mention that with just  
5 endosulfan alone, one illness injury is occurring as a  
6 result of exposures to the field residues. And then with  
7 endosulfan plus the others, out of 56 cases, 43 are  
8 occurring as a result of just exposure to field. That  
9 surprised me. Is that not well appreciated? I mean I  
10 would --

11           DPR STAFF TOXICOLOGIST BEAUVAIS: I'm not sure I  
12 understand the question.

13           PANEL MEMBER LANDOLPH: Well, I think it's  
14 fascinating data. And it surprised me that, you know, the  
15 levels were so high that when people are going out to  
16 harvest the crops, they're getting sick from exposure to  
17 this stuff. And is that well recognized within DPR?

18           DPR STAFF TOXICOLOGIST BEAUVAIS: Okay. I guess  
19 to clarify, when we -- these illness reports that we show  
20 here include the possible, probable, and confirmed. And  
21 in many cases they don't necessarily confirm that it was  
22 endosulfan or another chemical. But, you know, you can't  
23 necessarily know. But you go in and analyze field  
24 residues perhaps. These are -- so when we're talking  
25 about field residues, we're talking about folks that have

1 gone into harvest or to do some sort of field work  
2 afterwards. And it's on a field that was treated -- if  
3 it's included in here, it was treated with endosulfan and  
4 possibly two or three other compounds as well, possibly  
5 simultaneously or, you know, it's in a tank mix or  
6 sometimes over a period of days. Or the crew may have  
7 been in more than one field and then gotten sick. And so  
8 they're looking at what possible exposures they were at.

9 And so when you see these multi -- you know,  
10 endosulfan with other pesticides, this is a -- you know,  
11 we include it because it may be due to endosulfan, but we  
12 can't decide it for sure.

13 PANEL MEMBER BLANC: Can I ask why this section  
14 is in this volume, when I would have expected it to be  
15 under the "Human Exposure" -- "Human Illness" section?

16 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

17 PANEL MEMBER BLANC: Was there some -- I mean --

18 DPR STAFF TOXICOLOGIST BEAUVAIS: There may be a  
19 reason. I'm not -- I can tell you that the data are  
20 coming from the same branch that this -- and this is all  
21 worker health and safety data. And so it may be there for  
22 that reason. It's also included in the human health.

23 PANEL MEMBER BYUS: It's in the risk  
24 characterization as well.

25 DPR STAFF TOXICOLOGIST BEAUVAIS: It is in there

1 as well.

2 PANEL MEMBER BLANC: Where -- I was just  
3 looking --

4 PANEL MEMBER BYUS: Because I had some concerns  
5 about that too.

6 PANEL MEMBER BLANC: I was just looking at page  
7 86 where the human data are.

8 Is there another place in the risk -- in the  
9 medical toxicology in the --

10 PANEL MEMBER BYUS: Page 21 of the other volume.

11 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah, it's in  
12 both volumes.

13 PANEL MEMBER BYUS: "Reported Illnesses," page  
14 21.

15 PANEL MEMBER BLANC: Oh, I see. Gotcha.

16 Okay. Never mind.

17 PANEL MEMBER BYUS: If you'd read that.

18 PANEL MEMBER BLANC: I did see it.

19 PANEL MEMBER HAMMOND: It's hard to read.

20 PANEL MEMBER BLANC: But I got confused now.

21 PANEL MEMBER HAMMOND: You know, your  
22 presentation was all about airborne exposures.

23 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

24 PANEL MEMBER HAMMOND: And -- well, Ms. Fan  
25 stated a couple of ideas here. And one question is -- and

1 I can't remember if this holds for the airborne data.  
2 It's for a lot of the other data, the dietary data. There  
3 were corrections made for what percentage of crops were  
4 treated and there are various things about the decline --  
5 the use of this material has declined.

6 And actually the total amount used in California  
7 has declined quite a bit, correct?

8 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

9 PANEL MEMBER HAMMOND: Why is that?

10 DPR STAFF TOXICOLOGIST BEAUVAIS: It's a  
11 combination of newer chemicals coming into play and -- you  
12 know, the neonicotinoids, for example. And in the most  
13 recent decline in the 2004 to 2005 data, they attributed  
14 it very much to the decline in cotton acreage, which was  
15 one of the crops.

16 DPR ASSISTANT DIRECTOR JONES: This is Tobi  
17 Jones. Let me make one comment that was reflected in the  
18 discussion in our public meeting on this issue. And this  
19 was offered up by our representative from the County  
20 Agricultural Commissioners back in the -- and I'll look it  
21 up with Pam here -- probably the early nineties there was  
22 a substantial effort to reduce service water contamination  
23 with endosulfan. So --

24 PANEL MEMBER HAMMOND: Which contamination --

25 DPR ASSISTANT DIRECTOR JONES: Surface water

1 contamination because endosulfan is highly toxic to  
2 aquatic organisms.

3           And so the uses were more highly controlled at  
4 the county level through our permit system, and uses fell  
5 off as a result of that also.

6           PANEL MEMBER HAMMOND: Okay. This is kind of a  
7 question more for the Panel or for John. But one thing  
8 I've been a little unclear about as we think of a toxic  
9 air contaminant is how to think about something where the  
10 use is declining, but it's not really just one kind of  
11 decline. As I looked at the data, sometimes it goes up  
12 and sometimes it goes down. And some crops started using  
13 it more than other crops.

14           DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

15           PANEL MEMBER HAMMOND: And so the popularity of  
16 using a particular pesticide in a particular year  
17 shouldn't be driving whether or not something is a toxic  
18 air contaminant. And at some level if you want to think  
19 about what -- you know, if something's a toxic air  
20 contaminant, it may also depend on what the potential  
21 exposure would be if it were used more rather than -- you  
22 know. And I'm not sure how exactly we deal with that, but  
23 I want to put that out there; that a lot of the  
24 evaluations that have been done in the report are looking  
25 at what is the exposure today. But there are these --

1 although the ambient airs were based on ten years ago.

2 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

3 PANEL MEMBER HAMMOND: Right. And I do  
4 acknowledge that. But some of the other data were based  
5 on other things. And so I think that's one thing to -- at  
6 least we need to bear in mind as we look through these  
7 data.

8 DPR STAFF TOXICOLOGIST BEAUVAIS: Well, and  
9 actually the way that we adjust for the use -- and I  
10 showed you that slide with the use pattern, the percent  
11 that was used each month. And what's happening --

12 PANEL MEMBER HAMMOND: Yeah. But that's to get  
13 your annual.

14 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes. And  
15 that's the only point in which we're considering use in  
16 our exposure estimates is during -- is to determine what  
17 portion of the year might they be exposed. We're not  
18 dialing it down because --

19 PANEL MEMBER HAMMOND: Right, because you're not  
20 looking at how many people are exposed.

21 DPR STAFF TOXICOLOGIST BEAUVAIS: No. Right,  
22 exactly. And so that's -- and what happens as the use  
23 drops off is that it takes -- that tends to even out and  
24 you tend to have more months that go above 5 percent. And  
25 it just tends to, you know -- instead of having that tall

1 peak where, you know, you've got a 40 percent in two or  
2 three months, you end up with everybody getting a little  
3 closer to 20 percent or 10 percent. And so it tends to --  
4 we tend to actually estimate exposure more as the  
5 pesticide use drops off, for the annual exposure.

6 PANEL MEMBER HAMMOND: I had questions and  
7 comments about some things -- both the dietary and the  
8 reentry issues.

9 DPR STAFF TOXICOLOGIST BEAUVAIS: No, to clarify  
10 the dietary's going to be in the next portion.

11 PANEL MEMBER HAMMOND: That's what I wasn't clear  
12 about.

13 And the reentry, anything on that?

14 DPR STAFF TOXICOLOGIST BEAUVAIS: No, the  
15 reentry's here. So reentry --

16 PANEL MEMBER HAMMOND: This would be the time to  
17 talk reentry?

18 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

19 PANEL MEMBER HAMMOND: Okay. In the report, the  
20 comment is made that the reentry time for endosulfan is  
21 two days in California.

22 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

23 PANEL MEMBER HAMMOND: One day outside. But in  
24 California it's two days.

25 And then there's the pre-harvest interval, PHI.

1 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes.

2 PANEL MEMBER HAMMOND: I'm terrible at these  
3 acronyms.

4 Pre-harvest interval, and which might be for some  
5 crops as one day and some days are seven days.

6 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

7 PANEL MEMBER HAMMOND: You know, they're varying.  
8 And that's the -- that I think is based on the dietary  
9 issues, right?

10 DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah,  
11 controlling residues, yeah, right, exactly.

12 PANEL MEMBER HAMMOND: This is to control  
13 residues.

14 So that all makes sense. And then there's a  
15 statement made in the document a couple of times that when  
16 you're looking at reentry, you assume either it's the  
17 reentry interval of two days, or if the pre-harvest  
18 interval is longer, it's the pre-harvest interval time and  
19 then you add five to seven days to that.

20 DPR STAFF TOXICOLOGIST BEAUVAIS: Okay.

21 PANEL MEMBER HAMMOND: And --

22 DPR STAFF TOXICOLOGIST BEAUVAIS: I can clarify  
23 that.

24 Okay. To clarify, we use the reentry -- the  
25 restricted entry interval, the REI, which is the two-day

1 interval, for all activities except harvesting; because we  
2 assume that if you're harvesting a food crop, you're not  
3 going to harvest it before you can sell it, before it will  
4 have -- at a time when it would still have legal  
5 residues -- potentially have the legal residues.

6           So we set the harvesting at the pre-harvest --  
7 the expiration of the pre-harvesting interval. And for  
8 the short-term exposures we set it right at the expiration  
9 of each of -- of either the REI or PHI. But for the --  
10 again, for the -- when we're looking at these annual and  
11 seasonal estimates when we're looking at more of a typical  
12 exposure, there's no reason that people need to go in as  
13 soon as this expires time after time after time. So we  
14 assume that they don't go in right at the expiration  
15 period and we add a few days. And --

16           PANEL MEMBER HAMMOND: Well, it's like five to  
17 seven days, which the half-life is actually -- but on the  
18 other hand, it might well be that there's weaving or  
19 there's other -- I mean I don't know, but I would think  
20 that that's the kind of work that you'd almost --

21           DPR STAFF TOXICOLOGIST BEAUVAIS: And, again,  
22 this is only for the seasonal and annual.

23           PANEL MEMBER HAMMOND: And you almost have to  
24 talk to a agricultural specialist to know how the crops  
25 are handled. But it just concerned me, because that could

1 represent a significant underestimate.

2           And then going back to the comment that was made  
3 where there were illnesses reported that were related to  
4 reentry, that would also seem to create some of that  
5 problem.

6           So I just was concerned that that -- I mean maybe  
7 that's true. And I just don't know. But I -- in the lack  
8 of -- lacking knowledge, I would be setting -- I'd be  
9 using the two-day reentry. Except I understand for the  
10 pre-harvest. If it's harvesting, and entering the harvest  
11 crops would have to be after the pre-harvest interval.

12           DPR STAFF TOXICOLOGIST BEAUVAIS: Yeah.

13           PANEL MEMBER HAMMOND: But you don't say after  
14 that. You say five to seven days -- the pre-harvest  
15 interval plus five to seven days or the reentry plus five  
16 to seven days.

17           DPR STAFF TOXICOLOGIST BEAUVAIS: To try to get  
18 at a more typical event. And we --

19           PANEL MEMBER HAMMOND: But do we know that that's  
20 typical? I mean where does that come from that makes that  
21 typical?

22           DPR STAFF TOXICOLOGIST BEAUVAIS: What we know is  
23 when we have information from crop specialists about when  
24 certain events typically occur.

25           PANEL MEMBER HAMMOND: So that is how that was

1 done? For each crop the actual number of days was --

2 DPR STAFF TOXICOLOGIST BEAUVAIS: No. We know  
3 that weeding is done at a certain time. And it's going to  
4 vary by crop, you're right. And so we set an arbitrary  
5 interval that we expect is going to be shorter than when  
6 these activities -- you may need to only go in and weed by  
7 hand once or twice. I mean it's depending on the crop.  
8 It depends on the sensitivity of the crop and whether or  
9 not it can handle equipment. And, you know, it's going to  
10 vary widely.

11 PANEL MEMBER HAMMOND: I can certainly understand  
12 that that varies widely. And I certainly know it's  
13 outside of my -- the direct information's outside of my  
14 knowledge base.

15 DPR STAFF TOXICOLOGIST BEAUVAIS: And this is  
16 again only for the longer-term exposure estimates. We  
17 always have a short-term estimate that is done at the  
18 expiration of the REI or the PHI. There's always that.

19 PANEL MEMBER HAMMOND: Okay.

20 DPR STAFF TOXICOLOGIST BEAUVAIS: Whether or  
21 not -- and in some cases if we have no indication of  
22 long-term use -- or frequent use on a crop, then we don't  
23 do long-term estimates.

24 But we always have a short-term estimate. So  
25 that estimate is always there. So we always have an

1 estimate that involves --

2 CHAIRPERSON FROINES: I think, Kathy, if you have  
3 suggestions in this area, you should provide them to DPR,  
4 and that would be useful. I think that whether the  
5 specific recommendations have bearing on the MOE and the  
6 actual determination of TAC, you should state the  
7 implications when you provide the information.

8 PANEL MEMBER HAMMOND: Yeah. I mean because the  
9 other question I had in terms of toxic air contaminants --  
10 it sounds like it's an air exposure. But the crop residue  
11 is another exposure. Dietary's another one, which we'll  
12 get into. But on the other hand you have to look at  
13 people's total exposures, right, you know, when we're  
14 looking at the toxicity eventually. So is that the reason  
15 we're looking at these others as well -- these are the  
16 exposure routes -- so we have the full exposure, even  
17 though we're looking at a toxic air contaminant? We're  
18 not just -- we're saying, what is that adding to the base  
19 that the people have from other sources?

20 CHAIRPERSON FROINES: I think that -- that's why  
21 I'm a little hesitant about this right now, to tell you  
22 the truth, because it doesn't get factored in in terms of  
23 the actual numbers that form the basis of the MOE. And if  
24 it doesn't get factored in, then either we should tell  
25 them that that should happen or we should go with the

1 numbers that they have.

2           PANEL MEMBER HAMMOND: Well, that's part of what  
3 I was confused about and how to look at that.

4           CHAIRPERSON FROINES: And I think this is up to  
5 the panel, but my sense is that -- I don't really know  
6 what my sense is, because I think the issues you're  
7 raising are very good. I think my sense is that this  
8 becomes -- this issue and the dietary issue becomes  
9 something that one talks about qualitatively in terms of  
10 the fact that this may under-represent exposure to the  
11 public, but that the MOE gets calculated by the actual  
12 airborne concentrations that we have. But that's just my  
13 sense of it. I need -- you know, but we need to decide  
14 how we want to address that issue, because the way they're  
15 doing it is -- the way they have reached the designation  
16 of recommending this as a TAC has been based on the  
17 airborne concentrations and none of these other factors.  
18 And so it's up to the panel to decide what you think is  
19 most appropriate.

20           PANEL MEMBER LANDOLPH: Well, also in that second  
21 document, you got a nice five-page section on  
22 pharmacokinetics. Could you again -- I could recommend,  
23 please put some of the enzymology in and point out what  
24 the toxic metabolites result to be. It would be helpful.

25           CHAIRPERSON FROINES: What do you all think? I'm

1 trying to raise a question and I get absolute silence.

2 PANEL MEMBER BLANC: Well, I guess there's a -- I  
3 have a regulatory question in response to your question.

4 It's always been somewhat challenging, because  
5 the approach that we deal with outside of the pesticides  
6 is a completely different endpoint in the way in which the  
7 question is arrived at. And I'm not really -- it's not  
8 really clear to me that from a statutory -- I always  
9 understood it that the reason you have this sort of odd  
10 ratio with the 100 to 1 and 1,000 to 1 derived from a  
11 statutory guideline of some kind. But it's an internal  
12 DPR decision that that's how you do it? So if you wanted  
13 to do some kind of ratio that included the total body  
14 burden of exposure by all routes, you could do that too?  
15 And if the airborne exposure tipped you over to 100 to 1  
16 or 1,000 to 1, then that would still reach your threshold  
17 for recommending labeling as a toxic air contaminant?

18 DPR ASSISTANT DIRECTOR JONES: Well, I'm not sure  
19 I can answer your question directly, Paul. I think to be  
20 clear, DPR has chosen over the last two years to present  
21 to the Panel our comprehensive risk assessments, which  
22 cover the statutory requirements we have in other venues.  
23 I know sometimes that has created some discomfort for  
24 presenting you a lot information. That's why we didn't  
25 provide the complete appendix on the dietary analysis.

1 But it wasn't our intent to include that as a means of  
2 making a determination on presenting this as a toxic air  
3 contaminant. I mean I think prior to presenting --  
4 probably sulfuryl fluoride was the one we first did that,  
5 you know, where we split our documents.

6 So we basically had two risk assessments. And we  
7 had one focused on ambient air and one focused on all  
8 exposures, an aggregate consideration of inhalation,  
9 dietary, and occupational exposure.

10 So, you know, no, I don't believe that we  
11 would -- our regulation giving us a higher margin of  
12 exposure standard by which to make a determination on  
13 proposing a toxic air contaminant is based on ambient air  
14 exposure.

15 CHAIRPERSON FROINES: Based on what? I'm sorry.

16 DPR ASSISTANT DIRECTOR JONES: Based on ambient  
17 air exposure.

18 So the other information that we include in the  
19 document is our management's decision to present  
20 comprehensive risk assessments and not expend the  
21 resources to break out the ambient air exposure versus  
22 other routes of exposure.

23 And I think at the -- I mean I'm kind of posed to  
24 dilemma because of the discussion of Methidathion. I  
25 believe Dr. Byus was identifying that it was a good thing

1 that we included other exposures and considered aggregate  
2 exposures. So for kind of broad or regulatory purposes we  
3 are considering aggregate exposures. But for purposes of  
4 listing or proposing listing a compound as a toxic air  
5 contaminant, we're focusing on the ambient air exposure.

6 CHAIRPERSON FROINES: I would like -- Paul, I'd  
7 like to defer a discussion what came about to describe for  
8 a period of time between now and the next meeting. And  
9 I'll tell you what that is. Under AB 1807, there's a  
10 definition of a toxic air contaminant. That definition is  
11 very broad. It says that there may be the potential for  
12 health effects. And so it's -- as you know, it's a very  
13 broad -- the Legislature created a very broad definition.

14 DPR as a matter of policy uses the MOE. But  
15 there's no place in 1807 that says that there has to be an  
16 MOE to meet the criteria for a TAC. That's a DPR policy.  
17 And whether -- and we have disagreed with that for -- Stan  
18 and I --

19 PANEL MEMBER GLANTZ: Forever.

20 CHAIRPERSON FROINES: -- for 20 years.

21 (Laughter.)

22 CHAIRPERSON FROINES: And so I don't want to take  
23 it up now. It's an issue -- it's a matter of agency  
24 policy versus legislative mandate. And I'd rather deal  
25 with Methidathion -- endosulfan and deal with the legal

1 issues outside of here for at least this particular  
2 meeting.

3 Is that all right with you folks? It's a can of  
4 worms to get into right now.

5 PANEL MEMBER BLANC: Yeah, that's fine.

6 Well, then the answer I think would be that for  
7 the purposes of our discussion here, although it's too --  
8 it's in our interest and it's helpful to hear about the  
9 other scenarios of exposure, that in fact what we will  
10 focus on for right now will be the inhalation route of  
11 exposure.

12 CHAIRPERSON FROINES: Yeah, I think that your --  
13 see, if I had my choice about your documents, I would have  
14 a document that started out with some general information,  
15 and then from then on provided information that lead the  
16 agency to their conclusion. In other words, that it  
17 became focused, so that when you were seeing studies, the  
18 studies you were seeing were the studies that formed the  
19 basis for the ultimate decision; not a literature review,  
20 but a strategic document that said, "Here's how we got to  
21 this endpoint"; and it should be very focused.

22 So in that respect, what I'm doing is agreeing  
23 with you and saying that we don't really need to do  
24 dietary and --

25 PANEL MEMBER HAMMOND: -- crop residue.

1 CHAIRPERSON FROINES: What?

2 PANEL MEMBER HAMMOND: Crop residue --

3 CHAIRPERSON FROINES: -- crop residue issues.

4 And that DPR obviously disagreed with those in  
5 terms of having more than one document, as Tobi said. But  
6 my sense is that there should be -- you know, my guess  
7 wish list I would want a document -- when I wrote the lead  
8 standard, I wrote the whole -- the lead standard so it  
9 would go so that when you read the last sentence, you knew  
10 why you got there from the first sentence. And that seems  
11 to me to be the way we should do it.

12 PANEL MEMBER BLANC: But I do want to clarify  
13 something, because you had used the term "ambient air."  
14 But did you mean inhalation? Because doesn't the  
15 bystander -- in your terminology you differentiate between  
16 ambient air and bystander. But those are inhalation  
17 exposures and in fact --

18 DPR STAFF TOXICOLOGIST BEAUVAIS: That's correct.

19 PANEL MEMBER BLANC: -- the bystander inhalation  
20 exposures also are applicable to the determination of  
21 toxic air contaminant recommendation.

22 DPR ASSISTANT DIRECTOR JONES: Yes.

23 PANEL MEMBER BLANC: But I do want to clarify  
24 that.

25 There's something else I want to clarify. And it

1 may not be the point at which to do it. It may more  
2 reflect the third presentation. But the other scenario  
3 aside from dietary and bystander and occupational and  
4 ambient that you deal with is the swimmer scenario?

5 DPR STAFF TOXICOLOGIST BEAUVAIS: That's here.

6 PANEL MEMBER BLANC: And that consistent with  
7 this definition would not be relevant to our toxic air  
8 contaminant determination. However, based on the physical  
9 properties of this chemical and the fact that your  
10 toxicology data, which we're going to come to in the next  
11 talk, are clearer for inhalation and more potent for  
12 inhalation, wouldn't the route of exposure that would  
13 matter for a swimmer be inhalation of droplets and  
14 aerosols rather than the dermal exposure of a swimmer?  
15 Isn't the swimmer -- isn't -- no, not ingestion.

16 DPR STAFF TOXICOLOGIST BEAUVAIS: It's  
17 included -- inhalation is included in there.

18 PANEL MEMBER BLANC: So therefore is the --

19 DPR STAFF TOXICOLOGIST BEAUVAIS: This was based  
20 on EPA's model, the swim model, which includes inhalation  
21 and ingestion as well as dermal. So all three exposure  
22 routes are there.

23 PANEL MEMBER BLANC: So then does that -- does  
24 the swimmer -- therefore is part of the swimmer model --  
25 how do we know which part of that parse out in terms of --

1 isn't part of the swimmer model therefore applicable?

2 Your swimmer model came out with an MOE -- a low MOE,

3 right? Or is that wrong? Am I wrong about this?

4 DPR STAFF TOXICOLOGIST BEAUVAIS: I think that  
5 the exposures were very low in swimmers.

6 PANEL MEMBER BLANC: So that no matter how you  
7 cut it, the swimmer wouldn't have had a --

8 DPR STAFF TOXICOLOGIST BEAUVAIS: -- were fine,  
9 yeah.

10 PANEL MEMBER BLANC: Then it's probably not  
11 applicable.

12 And the model that you used that includes the  
13 inhalation piece of it takes into account the specifics of  
14 this chemical; is that correct? That varies by chemical?

15 DPR STAFF TOXICOLOGIST BEAUVAIS: Yes, it does.

16 PANEL MEMBER BLANC: Okay. Thanks.

17 CHAIRPERSON FROINES: Gary's gone. So just for  
18 the record, Gary Friedman has left for the day.

19 It's 12:43. Should we break until 1:30 for  
20 lunch?

21 PANEL MEMBER BLANC: Yes.

22 CHAIRPERSON FROINES: Yes. I don't think we need  
23 a motion. Let's just break.

24 So we're going to go then to the third speaker?

25 Cool.

1 Thank you.

2 (Thereupon a lunch break was taken.)

3 AFTERNOON SESSION

4 CHAIRPERSON FROINES: Welcome. We're ready to  
5 get started, so let's go.

6 DPR STAFF TOXICOLOGIST SILVA: Are we starting?

7 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

8 WOFFORD: Actually I've been asked for the public  
9 record to introduce myself.

10 I'm Pam Wofford from the Department of  
11 Pesticide --

12 CHAIRPERSON FROINES: Wait, wait, wait. Start  
13 over again.

14 PANEL MEMBER HAMMOND: I'm sorry. I apologize.

15 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

16 WOFFORD: I've been asked to introduce myself  
17 since I forgot to earlier.

18 PANEL MEMBER GLANTZ: We're just obsessing. It's  
19 okay.

20 DPR SENIOR ENVIRONMENTAL RESEARCH SCIENTIST

21 WOFFORD: My name is Pam Wofford. I'm with  
22 Department of Pesticide Regulation, the Environmental  
23 Monitoring Unit.

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

1 DPR STAFF TOXICOLOGIST SILVA: I'll be presenting  
2 evaluation of endosulfan as a toxic air contaminant.

3 --o0o--

4 DPR STAFF TOXICOLOGIST SILVA: And this slide  
5 summarizes the steps to the risk assessment process, and  
6 is a road map for my presentation.

7 Sheryl and Shifang already presented --

8 CHAIRPERSON FROINES: Marilyn, could you put the  
9 mic closer to your mouth. I can't hear you.

10 DPR STAFF TOXICOLOGIST SILVA: Sheryl and Shifang  
11 already presented the exposure assessment and fate. I'll  
12 be going through hazard ID and dose response assessment to  
13 identify the endpoints and the no-effect levels, or NOELs,  
14 for inhalation.

15 Finally, the risk characterization is generated  
16 through a culmination of information gained from the  
17 toxicology and the exposure, and these data determine the  
18 risk for humans.

19 --o0o--

20 DPR STAFF TOXICOLOGIST SILVA: The toxicology  
21 profile contains evaluations of all available toxicity  
22 studies for endosulfan, and they include acute studies  
23 submitted by DPR -- submitted to DPR by registrants,  
24 toxicity studies submitted to DPR to register under SB  
25 950, and literature studies.

1 --o0o--

2 DPR STAFF TOXICOLOGIST SILVA: These are the  
3 general pharmacokinetics for endosulfan.

4 The oral absorption according to a rat gavage  
5 study's 87 percent and is assumed to be 100.

6 Dermal absorption, 47.3. Sheryl's already talked  
7 about that.

8 Inhalation is assumed to be 100, and so on.

9 The primary metabolite is endosulfan sulfate.  
10 But also the diol and the lactone have been observed.

11 --o0o--

12 DPR STAFF TOXICOLOGIST SILVA: This just shows  
13 the pathway for endosulfan metabolism. And the sulfate is  
14 the main product, but you'll also see endosulfan diol and  
15 endosulfan lactone.

16 CHAIRPERSON FROINES: You have a mistake in at  
17 least one slide. The endosulfan diol is not CH3OH.

18 DPR STAFF TOXICOLOGIST SILVA: Oh, did I put  
19 that? Sorry. I can change that.

20 CHAIRPERSON FROINES: See here?

21 DPR STAFF TOXICOLOGIST SILVA: Oh, yeah. Sorry  
22 about that.

23 CHAIRPERSON FROINES: I passed my graduate  
24 orals --

25 (Laughter.)

1 --o0o--

2 PANEL MEMBER GLANTZ: I'm impressed, I have to  
3 say.

4 DPR STAFF TOXICOLOGIST SILVA: That he could see  
5 it? I know.

6 (Laughter.)

7 CHAIRPERSON FROINES: Normally when gamma-amino  
8 butyric acid, or GABA, binds its receptor, activating the  
9 GABA receptor, chloride ion binding complex, the chloride  
10 ions flow across the cell membrane to neutralize the cell  
11 interior and terminate fast signaling or cell excitation.

12 When endosulfan blocks the chloride channel, or  
13 otherwise interferes with the binding complex, the nerve  
14 stimulation remains, manifesting the clinical signs of  
15 neurotoxicity such as convulsions or tremors.

16 --o0o--

17 DPR STAFF TOXICOLOGIST SILVA: In the hazard  
18 identification section, we want to find the critical  
19 endpoint and do the NOEL selection. And this is done  
20 after having reviewed the available literature and  
21 identified the toxic endpoints.

22 We need to select the NOELs to calculate the  
23 risk. And these are referred to as the critical NOELs.  
24 They're generally the lowest NOEL, with the critical  
25 endpoint considered to be the most sensitive endpoint. So

1 that its use will protect other effects, for example,  
2 endocrine effects induced by endosulfan at higher doses.

3 We also look at the durations of exposure of the  
4 studies and select one that matches closest with human  
5 exposure duration.

6 --o0o--

7 DPR STAFF TOXICOLOGIST SILVA: These are the key  
8 studies for the acute endosulfan treatment. And the green  
9 shows the oral -- the oral NOEL, 0.7, in the rabbit  
10 developmental study. And there's also -- and that really  
11 doesn't come in very clearly on this, but it's an acute  
12 LC50 study. And there was no NOEL in that study, but  
13 there's a NOEL -- or a LOEL of 0.5.

14 Okay. So this study, while we didn't obtain a  
15 NOEL, will be used in the final decision on the NOEL for  
16 inhalation -- acute inhalation.

17 And, by the way, all these studies are used --  
18 are performed with a mixture of alpha- and  
19 beta-endosulfan.

20 --o0o--

21 DPR STAFF TOXICOLOGIST SILVA: In this slide, we  
22 ended up using finally the Subphrenic inhalation for our  
23 critical NOEL, but used also the acute LC50 study and the  
24 Subphrenic range finding. And the treatments are listed  
25 there and all the doses. And you might notice that the

1 LOELs for all three studies are very similar. But in the  
2 Subphrenic we didn't see any signs or effects before I  
3 think it's day 12. And -- or actually no effects prior to  
4 day 9. And yet all the LOELs were very similar for the  
5 three studies.

6 So we propose for the acute critical study to use  
7 the Subphrenic inhalation.

8 --o0o--

9 DPR STAFF TOXICOLOGIST SILVA: The advantages to  
10 the Subphrenic inhalation are the following:

11 All three LOELs were similar.

12 More animals were treated in the Subphrenic; 15  
13 per sex per dose versus 5 per sex per dose.

14 The Subphrenic used a 29-day recovery with 5 per  
15 sex per dose. And the acute had a 14-day observation  
16 after the dose.

17 0.194, which was the NOEL in the Subphrenic  
18 study, is reasonable based on the LOELs from the other  
19 studies -- or from all three studies.

20 And 0.194 is a conservative estimate for an acute  
21 NOEL, since acute NOELs are usually higher than Subphrenic  
22 or chronic NOELs.

23 And I'd like you to note that the three studies  
24 were from the same laboratory and in the same timeframe,  
25 within six months.

1 --o0o--

2 DPR STAFF TOXICOLOGIST SILVA: So the next is  
3 selecting the NOELs and endpoints for Subphrenic exposure.  
4 And the green shows the dietary, where we chose the two  
5 generation repro study with a NOEL of 1.18. And the red,  
6 again, is the same Subphrenic study that I mentioned  
7 before, with a NOEL of 0.194.

8 --o0o--

9 DPR STAFF TOXICOLOGIST SILVA: And here's a  
10 summary of the Definitive Subphrenic Inhalation Study.  
11 And as I showed before, it's aerosol, nose only.

12 And there are clinical signs of neurotoxicity,  
13 decreased body weight, decreased food, increased water  
14 intake, clinical chemistry effects that were reversed at  
15 the end of recovery.

16 --o0o--

17 DPR STAFF TOXICOLOGIST SILVA: For the chronic  
18 there were no inhalation studies available. However, for  
19 the dietary we used the one-year dog study with a NOEL.  
20 We went with the lower NOEL of 0.57.

21 --o0o--

22 DPR STAFF TOXICOLOGIST SILVA: So for the chronic  
23 NOEL we decided to go with the same Subphrenic inhalation  
24 in the rat. Only we extrapolated from Subphrenic to  
25 chronic to obtain an effective no-effect level.

1           So --

2           PANEL MEMBER LANDOLPH:  Could I ask you a quick  
3 question?

4           Could you please define ENEL in words.

5           DPR STAFF TOXICOLOGIST SILVA:  I did.  I got your  
6 comment.

7           PANEL MEMBER LANDOLPH:  Thank you.

8           DPR STAFF TOXICOLOGIST SILVA:  Its just  
9 Equivalent No-Effect Level.

10                               --o0o--

11           DPR STAFF TOXICOLOGIST SILVA:  The other  
12 endpoints:

13           Oncogenicity.  There was no evidence of  
14 oncogenicity in animal studies.

15           Genotoxicity.  We considered equivocal evidence  
16 from in vivo and in vitro gene tox studies.

17           And endocrine disruption.  Endocrine effects were  
18 observed in male rats only at doses surpassing neurotoxic  
19 doses.

20                               --o0o--

21           DPR STAFF TOXICOLOGIST SILVA:  The exposure  
22 assessment covers information already given by Sheryl.  
23 And for my work I used the corrected values that she  
24 showed previously.

25                               --o0o--

1 DPR STAFF TOXICOLOGIST SILVA: And this is a  
2 table that she already presented.

3 --o0o--

4 DPR STAFF TOXICOLOGIST SILVA: Because during the  
5 Methidathion panel discussion someone said that they  
6 appreciated seeing the aggregate exposure, I included this  
7 dietary summary, and chose for adults and infants the  
8 highest exposure in diet.

9 --o0o--

10 DPR STAFF TOXICOLOGIST SILVA: For the aggregate  
11 exposure to the public, I needed to look at the ambient  
12 air and the air for bystanders at work sites. So the air  
13 aggregate was the inhalation exposure plus the dietary  
14 exposure.

15 --o0o--

16 DPR STAFF TOXICOLOGIST SILVA: And here is, using  
17 Sheryl's data and the dietary data, the results of  
18 exposure -- aggregate exposure. And in parentheses there  
19 are -- it's the percentage diet of the overall exposure.  
20 And you can see that the diet comprises a pretty high  
21 percentage.

22 --o0o--

23 DPR STAFF TOXICOLOGIST SILVA: To characterize  
24 the risk, say, what is the risk to humans, we look at a  
25 combination of hazard identification, exposure assessment,

1 and uncertainty factors to determine the margin of  
2 exposure to characterize potential risk to humans.

3 --o0o--

4 DPR STAFF TOXICOLOGIST SILVA: The risk for  
5 non-carcinogenic health effects in humans is expressed as  
6 the margin of exposure, or MOE. The MOE is the ratio of  
7 the NOEL to the exposure level in humans.

8 The acute, Subphrenic, and chronic NOELs employed  
9 for the characterization of the risk exposure to  
10 endosulfan were derived from studies performed on  
11 laboratory animals.

12 When the NOEL is derived from an animal study,  
13 generally an MOE of at least a hundred is desirable  
14 assuming humans are ten times more sensitive than animals  
15 and that there's a tenfold variation in the sensitivity of  
16 the human population between the lower range of the normal  
17 population and sensitive subgroups.

18 In other words, we generally want the potential  
19 human exposure level to be at least a hundred times lower  
20 than the NOEL in animals.

21 Criteria for listing a pesticide as a TAC is when  
22 the MOE is less than 1,000 when based on an animal NOEL.

23 --o0o--

24 DPR STAFF TOXICOLOGIST SILVA: And here are the  
25 margins of exposure that we got for the inhalation groups.

1 And in green you can see all that are below 1,000, but all  
2 are greater than 100.

3 --o0o--

4 DPR STAFF TOXICOLOGIST SILVA: And then for the  
5 dietary, just for your information, the MOEs are very high  
6 for Subphrenic and chronic and over 100 for acute.

7 --o0o--

8 DPR STAFF TOXICOLOGIST SILVA: So just to give  
9 you a perspective here. To calculate the margin of  
10 exposure to the public where we have inhalation plus diet,  
11 the following is the formula we use.

12 --o0o--

13 DPR STAFF TOXICOLOGIST SILVA: And for aggregate  
14 air and diet for endosulfan we have the following MOEs:  
15 There's -- all of them are over 100 except for infant  
16 short-term bystanders.

17 --o0o--

18 DPR STAFF TOXICOLOGIST SILVA: So this is DPR's  
19 summary of the studies we're using, the critical studies  
20 for our NOELs. Dietary. And then on the bottom we're  
21 basically using one study for the acute/subchronic. And  
22 then we have a safe -- an additional 10X safety factor for  
23 the chronic.

24 --o0o--

25 DPR STAFF TOXICOLOGIST SILVA: And just for your

1 information also, this is what U.S. EPA is using.

2 They don't have a chronic NOEL for inhalation or  
3 an acute. So they're basically just using the Subphrenic  
4 as occupational for seasonal exposure to workers.

5 But you might note that our acute  
6 neurotoxicity -- or our acute NOEL for inhalation is much  
7 lower than the acute neurotox that they're using. And  
8 also our acute dietary is half as much, our Subphrenic is  
9 much lower, and our chronic is in the same ballpark as  
10 their dietary.

11 --o0o--

12 DPR STAFF TOXICOLOGIST SILVA: Focusing again on  
13 the air exposure. Here are the calculations for the  
14 reference concentrations. Air concentrations below the  
15 reference concentration, or RfC, are generally considered  
16 sufficiently low to protect human health.

17 The RfC's were calculated for acute seasonal and  
18 chronic exposure to endosulfan by dividing the inhalation  
19 NOEL by the respiratory rate in humans to obtain the  
20 equivalent human inhalation NOEL.

21 And at the bottom we have the -- Sheryl's already  
22 shown these -- the respiratory rates for infants and  
23 adults.

24 And, again, inhalation absorption is assumed to  
25 be 100 percent. Human equivalent inhalation NOEL was then

1 divided by an uncertainty factor of 100, described earlier  
2 when the NOEL is derived from animal data.

3 To convert RfC from microgram per cubic meter to  
4 parts per billion, the value was multiplied by the  
5 molecular volume and divided by the molecular weight of  
6 endosulfan.

7 --o0o--

8 DPR STAFF TOXICOLOGIST SILVA: So acute and  
9 Subphrenic RfC's are 3.3 microgram per cubic meter for  
10 infant, 6.9 microgram per cubic meter for adult. And the  
11 extrapolated values for chronic are a factor of ten less.

12 --o0o--

13 DPR STAFF TOXICOLOGIST SILVA: The DPR toxic air  
14 contaminant listing criteria is shown in this figure.  
15 Listing is considered when the exposure exceeds one-tenth,  
16 or 10 percent, of the reference concentration for acute  
17 and Subphrenic inhalation exposure to endosulfan.

18 This listing criteria limit is 0.2 parts per  
19 billion, 0.4 parts per billion in adult. And for chronic  
20 it's a factor of 10 lower. And I've shown micrograms per  
21 cubic meter in very tiny print there. And we will  
22 basically be regulating on the infant values, which are  
23 lower.

24 --o0o--

25 DPR STAFF TOXICOLOGIST SILVA: The risk

1 appraisal. Based on the previous slide, this table using  
2 the corrected exposure value shows the MOEs for the  
3 various exposure scenarios along with the percent RfC.  
4 The percentage should be approximately 10 percent or less  
5 in order to avoid listing as a TAC.

6 In red are the scenarios that do not exceed the  
7 threshold; that is, they're less than 10 percent. It's  
8 evident that the majority of conditions do though.

9 --o0o--

10 DPR STAFF TOXICOLOGIST SILVA: So the risk  
11 characterization summary using the corrected exposure  
12 values shows that the MOEs that are greater than a  
13 thousand are just ambient air, seasonal in infant and  
14 adult, and annual for adult.

15 But the majority of the MOEs are less than 1,000,  
16 ambient air for infant; bystander, all values.

17 Any questions?

18 CHAIRPERSON FROINES: I just have one question at  
19 the outset, and then I'll turn it over to Joe, who was the  
20 lead for it.

21 What are the elements in the MOE of a thousand?  
22 You have intraspecies and interspecies. And what's the  
23 other factor of 10?

24 DPR STAFF TOXICOLOGIST SILVA: That's -- I think  
25 that's the criteria for listing that the -- where is that?

1           Okay. For DPR the criteria for listing is when  
2 exposure exceeds one-tenth, or ten percent, of the  
3 reference concentration. One-tenth of the reference  
4 concentration. So it's a thousandfold. So you have  
5 interspecies, intraspecies, and then an additional tenfold  
6 below the reference dose. So that's a thousand.

7           CHAIRPERSON FROINES: Okay. Can you and perhaps  
8 Melanie help me. Because in the OEHHA comments, they  
9 suggest in calculating an RfC OEHHA would add an  
10 uncertainty factor to protect infants and children due to  
11 their greater sensitivity to the endocrine disrupting and  
12 neurotoxic effects of Endosulfan. So it sounds as though  
13 this factor of ten is not part of your thousand.

14           DPR STAFF TOXICOLOGIST SILVA: No, I think  
15 that -- I don't really know about their extra 10X factor.

16           DPR ASSISTANT DIRECTOR JONES: Just let me  
17 clarify.

18           The proposed listing criteria is an additional  
19 tenfold safety factor. It doesn't have anything to do  
20 with OEHHA's recommendation. So I mean I think that is a  
21 separate issue.

22           OEHHA DEPUTY DIRECTOR ALEXEEFF: George Alexeeff  
23 with OEHHA.

24           Yeah, just as a clarification, I think what DPR  
25 is describing is their normal procedure for listing

1 something as a toxic air contaminant. It simply adds a  
2 tenfold -- if it's within tenfold of the margin of  
3 exposure, then that's a condition to allow them to proceed  
4 in the regulation to list.

5 For calculating the RfC, well, they can describe  
6 how they calculated it, which is a slightly different  
7 matter. Okay?

8 CHAIRPERSON FROINES: I don't know.

9 OEHHA DEPUTY DIRECTOR ALEXEEFF: Well, the RfC  
10 they calculated -- I don't want to put words and describe.  
11 But as I understand, the RfC they calculated used the  
12 standard two uncertainty factors. So --

13 CHAIRPERSON FROINES: But why -- I'm confused.  
14 What is the policy of DPR and OEHHA on a tenfold safety  
15 factor for children?

16 DPR STAFF TOXICOLOGIST SILVA: According  
17 to -- the infants and children is a different issue, and  
18 that's not something that we deal with at DPR.

19 The criteria for identifying pesticides as a  
20 toxic air contaminant, do you want me to read that?

21 CHAIRPERSON FROINES: (Shakes head.)

22 I mean maybe the Panel does, yes. I know it.

23 Go ahead with the criteria.

24 DPR STAFF TOXICOLOGIST SILVA: Do you want me to  
25 read this?

1 CHAIRPERSON FROINES: Yeah, please read it.

2 DPR STAFF TOXICOLOGIST SILVA: Okay.

3 "A pesticide shall be identified as a toxic air  
4 contaminant if it's concentrations in ambient air are  
5 greater than the following levels: (For the purposes of  
6 this section, a threshold is defined as the dose of a  
7 chemical below which no adverse effect occurs.)

8 "For pesticides which have thresholds for adverse  
9 health effects, this level shall be tenfold below the air  
10 concentration which has been determined by the Director to  
11 be adequately protective of human health.

12 "For pesticides which do not have thresholds for  
13 adverse health effects, this level shall be equivalent to  
14 the air concentration which would result in a tenfold  
15 lower risk than that which has been determined by the  
16 Director to be a negligible risk."

17 CHAIRPERSON FROINES: And is that a regulation?

18 DPR ASSISTANT DIRECTOR JONES: It's not a policy.  
19 It's a regulation.

20 CHAIRPERSON FROINES: It's a regulation that you  
21 passed?

22 DPR ASSISTANT DIRECTOR JONES: Yes.

23 PANEL MEMBER BLANC: Well, that answers the  
24 question I had earlier, doesn't it?

25 CHAIRPERSON FROINES: What's that?

1 PANEL MEMBER BLANC: That was the question I was  
2 trying to ask earlier, I think.

3 CHAIRPERSON FROINES: Go ahead.

4 PANEL MEMBER BLANC: You know, before lunch I  
5 asked whether it was policy or regulation. It sounds like  
6 the answer is it's regulation, the hundredfold business.

7 PANEL MEMBER GLANTZ: Right. But it's their  
8 regulation. It's not law. It's their regulation. Which  
9 I'm being very restrained because we've had huge fights  
10 about this in the past.

11 CHAIRPERSON FROINES: Well, I'm just -- George,  
12 then I'm confused. Why would you have put this  
13 recommendation into your findings if you knew what has  
14 just been said? It seems like you're making a  
15 recommendation for which there's no apparent basis or  
16 there's -- I don't know. Help us here.

17 OEHHA DEPUTY DIRECTOR ALEXEEFF: I'd be happy to  
18 help you.

19 Okay. So the problem is we're a little bit --  
20 and Tobi can help clarify in case I'm a little off base.  
21 But there's a little bit of confusion between the  
22 regulatory basis that Department of Pesticide Regulation  
23 uses for determining that something is a toxic air  
24 contaminant versus the risk assessment procedure.

25 So, the comments that we submitted are on the

1 risk assessment procedure and are not commenting on the  
2 regulation that had been developed. So what we're  
3 referring primarily there is development of a reference  
4 dose. So if -- our comments on that has to do with how we  
5 felt the margin of safety or of the uncertainty for  
6 calculating the reference dose. That's what is being  
7 referred to there.

8           So I don't know if that helps clarify. We'd be  
9 happy to explain why we have that opinion, if that's the  
10 question that you'd like us to answer right now.

11           CHAIRPERSON FROINES: Well, having gone through  
12 SB 25, we know why you have this opinion.

13           OEHHA DEPUTY DIRECTOR ALEXEEFF: Okay. Well, I  
14 thought the specific reasons for this particular compound,  
15 if that --

16           CHAIRPERSON FROINES: Yeah, go ahead.

17           OEHHA DEPUTY DIRECTOR ALEXEEFF: I'll have our  
18 staff person -- I mean Dr. David Ting, he's our new  
19 section chief for our branch -- our section that reviews  
20 the Department of Pesticide Regulation risk assessments.

21           OEHHA RISK ASSESSMENT BRANCH CHIEF TING: Hi. My  
22 name is David Ting and I'm with OEHHA.

23           OEHHA agrees with the toxicology evaluation  
24 carried out by DPR. And we agree with the selection of  
25 the critical animal studies and identification of the

1 NOELs in the risk assessment. However, after looking at  
2 some of the red studies that indicate young animals could  
3 be more sensitive to some of the health effects resulted  
4 from endosulfan exposure, OEHHA would apply an additional  
5 uncertainty factor to the risk assessment.

6 CHAIRPERSON FROINES: Thank you.

7 So I understand, so that the issue is a risk  
8 assessment approach, methodology, policy, however you  
9 describe it, compared to what the regulatory requirements  
10 are for DPR. Is that a correct way of saying it?

11 OEHHA DEPUTY DIRECTOR ALEXEEFF: Correct. So  
12 whatever the -- George Alexeeff. Whatever the resulting  
13 number is, in this case as Dr. Silva read about the  
14 significant risk that's determined by the Director. We  
15 would suggest the significant risk level should be  
16 threefold lower based -- not threefold? -- whatever --  
17 some additional factor lower to protect infants and  
18 children. And then the regulatory requirement would play  
19 out the way it normally would. That's to try to resolve  
20 the confusion.

21 CHAIRPERSON FROINES: Yeah, that would require a  
22 change in their regulation.

23 OEHHA DEPUTY DIRECTOR ALEXEEFF: No, we're not  
24 changing their regulation, no. She could read the  
25 regulation again to clarify it. It basically says that

1 they apply an additional tenfold factor to the level  
2 determined to be -- an insignificant risk or significant  
3 risk? -- by the Director.

4 DPR ASSISTANT DIRECTOR JONES: Significant risk.

5 DPR STAFF TOXICOLOGIST SILVA: Wait.

6 PANEL MEMBER BYUS: Negligible.

7 OEHHA DEPUTY DIRECTOR ALEXEEFF: Negligible risk?

8 DPR STAFF TOXICOLOGIST SILVA: To be -- yes.

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

10 DPR STAFF TOXICOLOGIST SILVA: -- determined by  
11 the Director to be a negligible risk.

12 PANEL MEMBER GLANTZ: So, John, I think what  
13 they're saying is that the -- the difference in opinion is  
14 what level of exposure constitutes a negligible risk. And  
15 OEHHA's suggesting that should be a lower number than DPR  
16 is, because they're saying that you need to take into  
17 account that -- not only the differences in breathing rate  
18 with infants, but at the same level of exposure there's  
19 going to be a bigger effect in the infant.

20 And then after you have that, then the regulation  
21 sort of sets where you put the line. So they're changing  
22 the risk estimate that is then applied to the -- the  
23 regulation is then applied to. They're not differing on  
24 what the regulation is.

25 Is that right?

1           OEHHA DEPUTY DIRECTOR ALEXEEFF: Correct. Yeah,  
2 we're not changing. We're just raising an issue with  
3 regards to the risk, yes.

4           PANEL MEMBER GLANTZ: So that explains the thing  
5 you were asking me about.

6           It's a very soothing noise, wherever it's coming  
7 from.

8           PANEL MEMBER BYUS: Puts you right to sleep.

9           CHAIRPERSON FROINES: Are there any comments on  
10 this particular issue before we go ahead?

11           Joe?

12           PANEL MEMBER LANDOLPH: On this specific issue?

13           CHAIRPERSON FROINES: No.

14           PANEL MEMBER LANDOLPH: Or generally?

15           Yeah, I want to comment.

16           Yeah, I wrote some comments, about three pages,  
17 and I gave them to DPR. And I'll just try and summarize  
18 them.

19           You know, I want to congratulate Marilyn and  
20 colleagues for writing such a huge document. It's a lot  
21 of hard work. In general it's pretty well written.  
22 Wherever possible, if you can, I'd recommend some  
23 condensation just by a little more concise writing,  
24 because otherwise -- well, this is a problem with every  
25 document that gets big. It kind of puts you to sleep if

1 it's not a little bit concise. So do the best you can.

2           Regarding the chronic -- the toxicity and the  
3 oncogenicity studies, I went and did a hazardous database  
4 substance search and a tox line search. And they seem to  
5 indicate that -- I guess it's EPA according to the  
6 American Conference of Government Hygienists calls  
7 endosulfan not classifiable, A4, as to carcinogenicity.  
8 So you might want to put that statement in there  
9 discreetly somewhere. That doesn't mean it's not a  
10 carcinogen. It just means the database is not good enough  
11 to decide one way or the other.

12           And I would buff that up, and I'll give you some  
13 more comments there.

14           On your discussion of the genotoxicity, I would  
15 recommend revisiting the way you look at that data. In my  
16 opinion -- on page I guess it was 64 or so there's a big  
17 table where you have a lot of data. And that data  
18 indicates about 12 of the 25 tests -- 13 of the 25 tests  
19 are positive. So to me as a genetic toxicologist, I  
20 wouldn't call that negative or equivocal. I think there's  
21 data there.

22           And when you look at different types of  
23 genotoxins, sometimes some are odd like this. They don't  
24 show up in every test. That just means they have a more  
25 specific mechanism of action. So I think it is genotoxic.

1           And you have statements in here that it forms DNA  
2 adducts too.

3           So I think it is genotoxic. And I'd recommend  
4 you revisit that in your writing, both in the executive  
5 summary and in the text. And I made some suggestions as  
6 to how to help you out there.

7           I'm convinced that it causes, from your writing  
8 and the literature, chromosome aberrations, micronuclei,  
9 and mitotic gene conversion and reverse mutations in  
10 yeast. And that's all positive.

11           It also does inhibition of gap junctional  
12 communication. It's a tumor promoter. Now, that hasn't  
13 yet crossed the line into a carcinogen until the studies  
14 really show that definitively it is. But it's worrisome  
15 that it's got some genotoxic activity and tumor promoting  
16 activity. So just mark it as it is. It's not going to  
17 change your risk assessments now, because you can't do  
18 that until you get carcinogenicity data. But I would bulk  
19 those sections up and list them a little bit more  
20 specifically.

21           Let's see, what else?

22           Oh, and you go through the FIFRA acceptable many  
23 times. Tell you the truth, I don't know what FIFRA  
24 acceptable is. Are there concise guidelines?

25           DPR STAFF TOXICOLOGIST SILVA: Yes.

1 PANEL MEMBER LANDOLPH: Maybe you might want to  
2 append those to the document or something.

3 And I don't -- this is a personal bias. I  
4 wouldn't throw a study out just because it's not FIFRA  
5 acceptable. I would --

6 DPR STAFF TOXICOLOGIST SILVA: No, that's  
7 not -- one of the things about FIFRA studies that's very  
8 useful is that there are specific guidelines. And so you  
9 know exactly what there is. Everything is complete. You  
10 have all the -- you have acquired a number of animals.  
11 You have a required protocol. There's quality assurance,  
12 there's GLP. There are individual data for each animal  
13 for every parameter.

14 And then, one of the purposes of the FIFRA  
15 studies is to get a NOEL, which often times in literature  
16 studies they're not looking for specifically a NOEL but  
17 they're looking for, you know, one certain aspect.

18 No, but we don't --

19 PANEL MEMBER LANDOLPH: Yeah, just the reason I  
20 bring this up, it's just mentioned so many times, it gives  
21 the reader the impression that you're trying to knock out  
22 studies that are not FIFRA acceptable. I mean certainly  
23 you can weight them downward. That's okay. But maybe one  
24 way to do it is just put it in parentheses or something  
25 like that, so you have to say it so many times.

1 DPR STAFF TOXICOLOGIST SILVA: Okay.

2 CHAIRPERSON FROINES: Wait. I'm sorry. They  
3 cannot weight studies down that aren't FIFRA guidelines.  
4 Absolutely not.

5 PANEL MEMBER LANDOLPH: Well, if you're convinced  
6 they're fatally --

7 CHAIRPERSON FROINES: The problem we have here is  
8 that what they're doing is they're mixing 950 documents  
9 with 1807 documents -- 1807 process.

10 Pardon me?

11 PANEL MEMBER HAMMOND: Translate.

12 CHAIRPERSON FROINES: There is nothing in 1807  
13 that requires the use -- that a paper meet FIFRA  
14 guidelines. There is no requirement. That does not --  
15 the definition, as I said earlier, of a toxic air  
16 contaminant is very clear, it's very broad. There is not  
17 a word in AB 1807 that says you have to have FIFRA  
18 guidelines. They have to -- in fact, what is -- the  
19 criteria that this panel uses for determining the quality  
20 of studies is whether they are in the peer-reviewed  
21 literature, right? That's always been our policy, and  
22 I've been on this Committee since '83.

23 So since 1983 the criteria has been peer-reviewed  
24 publications and not reports. And 1807 doesn't require  
25 FIFRA guidelines. Therefore, the trouble with pushing

1 these two documents into one is they're using the FIFRA  
2 guideline requirement under 950 but it's not in ours. So  
3 that we end up having to read all that stuff about FIFRA,  
4 when in fact it's not a requirement under 1807.

5           And therefore it would be much better -- and  
6 we've talked about this in the past -- if we had two  
7 documents. I mean word processors would seem to be able  
8 to take something out of here and put it in another  
9 section. Right? It seems to me that that's a word  
10 processing problem, so that we wouldn't have to read  
11 under -- I mean in this document it was almost every  
12 paragraph talked about FIFRA guidelines. And it's not a  
13 requirement. Okay.

14           So it does mean that we have the problem of  
15 having to go through for \$100 a meeting an enormous number  
16 of sections which has nothing to do with this Panel.  
17 Which we shouldn't really have to do. We shouldn't have  
18 to read occupational studies in here.

19           DPR ASSISTANT DIRECTOR JONES: John, I'll carry  
20 back to my managers your desire to see a separate  
21 document. We will continue to use studies that we receive  
22 in DPR that we have to make a determination on  
23 acceptability under the SB 950 statutory language.

24           CHAIRPERSON FROINES: Sure. I'm not quarreling  
25 with that at all.

1 DPR ASSISTANT DIRECTOR JONES: But I think in  
2 order that -- let me just say one thing to Joe.

3 Joe, I would be reluctant to advise Marilyn to  
4 include the FIFRA guidelines because it's very voluminous,  
5 and you're after trying to get us to reduce documents. We  
6 can provide a web link to both EPA's data requirements,  
7 which DPR uses, and to the guidelines which provide  
8 guidance to those conducting the studies.

9 PANEL MEMBER BYUS: I have a question.

10 CHAIRPERSON FROINES: Go ahead. I'm sorry.

11 PANEL MEMBER BYUS: Your stakeholder toxicity  
12 studies, you know, the ones that aren't in the public  
13 literature, are they FIFRA guidelines? Do they follow  
14 FIFRA guidelines?

15 DPR ASSISTANT DIRECTOR JONES: What do you mean  
16 stakeholder --

17 PANEL MEMBER BYUS: Don't you have the -- you  
18 know, don't your stakeholders do toxicity studies  
19 themselves and then, you know, they have that -- the  
20 database that you use, there's a database of animal  
21 toxicity studies and --

22 DPR ASSISTANT DIRECTOR JONES: Right. And based  
23 on individual companies, they may or may not publish  
24 those, you know. But they don't -- they are not required  
25 to publish those, but they are required to present them to

1 us.

2 PANEL MEMBER BYUS: Right. But are they FIFRA --  
3 do they use FIFRA guidelines or not? All of them? Is  
4 there a policy -- I mean it's just a statement.

5 DPR ASSISTANT DIRECTOR JONES: Not to dwell on  
6 this, but a law contemporaneous with 1807 required us to  
7 have studies that were acceptable under the FIFRA  
8 guidelines. We have a term, "complete valid inadequate."  
9 It's in the law, that we had to go through and judge the  
10 studies.

11 CHAIRPERSON FROINES: The what? I'm sorry.

12 DPR ASSISTANT DIRECTOR JONES: And we continue to  
13 receive those studies from registrants who want to  
14 register compounds in California.

15 CHAIRPERSON FROINES: What did you say about 1807  
16 and FIFRA?

17 DPR ASSISTANT DIRECTOR JONES: I said a law  
18 contemporaneous with 1807.

19 CHAIRPERSON FROINES: Oh, contemporaneous. But  
20 it's contemporaneous --

21 PANEL MEMBER BYUS: They do use -- when they  
22 provide these studies, they must follow FIFRA guidelines.

23 DPR ASSISTANT DIRECTOR JONES: That's right.

24 PANEL MEMBER BYUS: And you said -- and she's  
25 saying yes. That's what I --

1           DPR ASSISTANT DIRECTOR JONES: On an individual  
2 basis we may consider studies that are presented in the  
3 scientific literature, we may consider studies that are  
4 done under the guidelines for European Union. But I think  
5 that's -- in answer to your question, yes, they use those.

6           PANEL MEMBER LANDOLPH: And then just a few more  
7 quick comments.

8           CHAIRPERSON FROINES: Wait. Let me just -- since  
9 I started this. I think within the context of our  
10 criteria of peer-reviewed studies, we should know whether  
11 a study is peer reviewed or not. And if it's a company  
12 study, we should know that. Because if we know it's a  
13 report, we may weigh that differently than a peer-reviewed  
14 study. And that's -- see, that's the difference we have  
15 here. We have a 950 where the FIFRA guidelines are the  
16 key factor. But this Panel hasn't worked that way. And  
17 so there's this paper, for example, that wasn't in the  
18 document, genotoxic effects of endosulfan and  
19 beta-endosulfan on human HEPG2 cells. This is in  
20 environmental health perspectives. This paper was not in  
21 the document. It clearly is a good, solid peer-reviewed  
22 publication.

23           DPR STAFF TOXICOLOGIST SILVA: I think -- I wrote  
24 in an e-mail to you that I just missed it. And it was not  
25 left out because it wasn't a FIFRA guideline study. I

1 just missed it.

2 CHAIRPERSON FROINES: Oh.

3 PANEL MEMBER BLANC: Joe, do you want to finish  
4 up your thing too?

5 PANEL MEMBER LANDOLPH: Yeah, thank you. I'll be  
6 brief.

7 And I would recommend under biotransformation --  
8 again, it's throughout the whole document, this is Part  
9 2 -- that you please list and refer to the enzymes that  
10 metabolize endosulfan, whether they're P-450s or other  
11 enzymes, which ones, and glutathione transferases and  
12 which ones. And there's a statement that these enzymes  
13 were induces non-specifically. I didn't know what that  
14 meant. You might -- if you could clarify that for us,  
15 that would help.

16 And then pull forward into the executive summary,  
17 and I would recommend a concise capsulation of the  
18 genotoxicity studies and the gap junctional communication  
19 inhibition in the tumor promotion studies, just very  
20 concisely.

21 And I think that would take care of it. And  
22 thank you.

23 CHAIRPERSON FROINES: Paul.

24 PANEL MEMBER BLANC: I have a question that  
25 doesn't pertain directly to your presentation, but it just

1 pertains to material here.

2 But before I go there, the first slide that you  
3 showed that related to studies that you selected, and  
4 there was the inhalation --

5 DPR STAFF TOXICOLOGIST SILVA: Oh, the table?

6 PANEL MEMBER BLANC: It was like the sixth slide  
7 or something. There was an inhalation study that you  
8 summarized. But then in the end that wasn't the  
9 inhalation study that you used.

10 Before the Subphrenic.

11 DPR STAFF TOXICOLOGIST SILVA: The acute --

12 PANEL MEMBER BLANC: The acute rat where all the  
13 doses -- there was a LOEL but no NOEL.

14 DPR STAFF TOXICOLOGIST SILVA: Right.

15 PANEL MEMBER BLANC: And then you didn't end up  
16 using this. You ended using the Subphrenic. But you said  
17 this study was from the same lab as the Subphrenic?

18 DPR STAFF TOXICOLOGIST SILVA: Yes.

19 PANEL MEMBER BLANC: And because that study did  
20 have a NOEL and this only had a LOEL, you preferred to use  
21 that?

22 DPR STAFF TOXICOLOGIST SILVA: Yes.

23 PANEL MEMBER BLANC: But what wasn't completely  
24 clear to me was, had you used this LOEL and then done the  
25 extrapolation to get to a NOEL, what would the number have

1 been?

2 DPR STAFF TOXICOLOGIST SILVA: Well --

3 PANEL MEMBER BLANC: You would use a factor of  
4 10?

5 DPR STAFF TOXICOLOGIST SILVA: Well, in general,  
6 yes. But the thing is is usually the acute NOELs are  
7 higher than the Subphrenic. And so that's why, you know,  
8 in the past we've just used the Subphrenic NOEL. And  
9 based on the three --

10 PANEL MEMBER BLANC: But wouldn't this then be  
11 .056?

12 DPR STAFF TOXICOLOGIST SILVA: Yeah.

13 PANEL MEMBER BLANC: And what is the one that you  
14 got based on the --

15 DPR STAFF TOXICOLOGIST SILVA: .19.

16 PANEL MEMBER BLANC: So this would be 50 percent  
17 less if you used this?

18 And so your rationale other than it giving you a  
19 lower number is what?

20 DPR STAFF TOXICOLOGIST SILVA: Well, okay, if you  
21 look at the Subphrenic study, you can see that even on a  
22 Subphrenic basis -- and I think you need to go up another  
23 couple of slides. Up the other way, yeah.

24 See, if you look at the Subphrenic, you'll see  
25 that you're not seeing any effects prior to day 9. And

1 that was at .387, which is the LOEL. Whereas, at 0.44 in  
2 the range finding, which was not a detailed study, that  
3 was just, you know, a summary, but they had these effects.  
4 So at .44 you're seeing decreased body weight gain.

5           And then the LOEL for the acute, which was .567.  
6 And that dose was used only in females. You can see that  
7 there are a lot of effects at that slightly higher dose.  
8 At 28 minutes females are showing clinical signs  
9 neurotoxicity.

10           So it seems like it's a reasonable selection for  
11 a NOEL considering the effects you see on a Subphrenic  
12 study, that, you know, going from .38, .44, .57, how steep  
13 that is, it seems very reasonable to choose .194 as a  
14 NOEL.

15           PANEL MEMBER BLANC: But let's say you had two  
16 studies that weren't from the same lab and one was an  
17 acute study and one was a Subphrenic study, and the  
18 Subphrenic study said, "Well, we didn't see anything at  
19 dose" -- oh, let me make it an even clearer example.  
20 Suppose you had two acute studies, and one had an apparent  
21 NOEL that was at .1 but the other one had a -- didn't have  
22 it. I mean I'm not sure that you have a rational basis  
23 for discounting the study at which you have the one acute  
24 study that you have, which has a LOEL but not a NOEL, and  
25 instead using the NOEL from a study which wasn't designed

1 to look at acute effects even though it has some comments  
2 on what happened in the first nine days.

3 DPR STAFF TOXICOLOGIST SILVA: Okay. Look at  
4 the -- could you go to the next slide.

5 No, back. Yeah.

6 The advantages to using that I listed here, that  
7 how similar the three NOELs were but how steep the curve  
8 seemed. But also in the Subphrenic study we're treating  
9 15 per sex per dose along with a 5 per sex per dose  
10 follow-up, versus the acute where there's only 5 per sex  
11 per dose used.

12 PANEL MEMBER BLANC: But I'm not sure that I  
13 would be compelled either because of what -- you're seeing  
14 an effect. That would be a compelling argument to me if  
15 you had -- if you were making the reverse argument and  
16 trying to say that something was a no-effect level in a  
17 study with only 5 and then you had 15 where you saw an  
18 effect, because there'd be a statistical -- more of a  
19 statistical chance of not seeing an effect in only 5.

20 DPR STAFF TOXICOLOGIST SILVA: But then you're  
21 not seeing anything on a Subphrenic basis of .19.

22 PANEL MEMBER BLANC: But it was a study designed  
23 to do different things. I mean am I -- are you  
24 assured -- but let me ask the question again the way I  
25 would.

1           If you still -- if you had two studies, one of  
2 which didn't see something but the other one which did --

3           DPR STAFF TOXICOLOGIST SILVA: Okay. You're  
4 going to have to be looking at, you know, when it was  
5 done, the lab it came out of, how many animals they used,  
6 a lot of things. I mean it just depends. You know, I  
7 have to look at the studies.

8           PANEL MEMBER BLANC: I know.

9           Does anybody else have the same question that I  
10 have? Is this -- I mean I'll drop it if I'm out of line.

11          CHAIRPERSON FROINES: Craig.

12          PANEL MEMBER BYUS: I don't have any problems  
13 with it. I think it's fine. I mean I think it's a matter  
14 of judgment. And this LOEL versus NOEL, I mean obviously  
15 when you have the low effects and then trying to  
16 extrapolate to no effects is not as satisfying always as  
17 something that actually -- a series of doses where someone  
18 actually measured no effects. That's the other issue.

19          So I mean I think it's always a -- it's a  
20 judgment here and, you know, I don't think it's that far  
21 off I mean without getting all the -- you know, reading  
22 all the studies in detail. I mean it's rational.

23          DPR STAFF TOXICOLOGIST SILVA: Yeah, there just  
24 aren't many studies out there at all on inhalation for  
25 endosulfan.

1           PANEL MEMBER BLANC: No, I understand. The  
2 reason I asked the whole series of questions is since it's  
3 a 50 percent lower level than if I carry the math through  
4 for things for which you had a ratio of a thousand five  
5 hundred, which you say wouldn't cut muster to be a TAC  
6 recommendation, now would suddenly be less than a  
7 thousand. So I don't know how -- I don't remember exactly  
8 how close some of your numbers were. So --

9           DPR STAFF TOXICOLOGIST SILVA: Actually though  
10 there's no short term for the ambient air. Only for  
11 bystanders. And those were all less than a thousand --

12           PANEL MEMBER BLANC: -- anyway.

13           DPR STAFF TOXICOLOGIST SILVA: Yeah.

14           PANEL MEMBER BLANC: Okay. So let me ask my  
15 other question, which was just the question that didn't  
16 refer to your slides. It has to do with mechanism, which  
17 as I understand it is -- as you emphasize, the  
18 GABA-mediated pathway. Why is it that in some of the  
19 animal studies there were decreased acetylcholinesterase  
20 levels? And it was in more than one of your studies. You  
21 don't comment on it at all. It's just reported, and I  
22 was --

23           DPR STAFF TOXICOLOGIST SILVA: It was mainly in  
24 the Subphrenic rat study. And we didn't see it in the  
25 chronic. It was -- you know, I added all that, but those

1 things weren't observed in later studies. It doesn't seem  
2 to be --

3 MEMBER BLANC: And it's in the cat study too,  
4 right, your report?

5 DPR STAFF TOXICOLOGIST SILVA: But wasn't  
6 that -- I think that was like an IV study or a really  
7 unusual route.

8 PANEL MEMBER BLANC: Yeah, but I mean -- yeah,  
9 but I just didn't -- I was completely confused by it and  
10 thought, boy, did I -- was there some section I missed  
11 here about its mechanism of action?

12 DPR STAFF TOXICOLOGIST SILVA: I don't think so.  
13 I think --

14 PANEL MEMBER BLANC: I think that it would be  
15 worth having a couple of sentences that say, "Although  
16 this was observed, it wasn't consistent. We don't think  
17 that it's" -- because otherwise it's just hanging out  
18 there.

19 DPR STAFF TOXICOLOGIST SILVA: Okay.

20 PANEL MEMBER BLANC: And then in terms of the  
21 human health effects, I know that the pesticide illness  
22 reporting system appears two different places. We've  
23 already commented on this before. The way those data are  
24 described, they're pretty useless from a human health  
25 understanding, because systemic, skin, eye --

1 DPR STAFF TOXICOLOGIST SILVA: Yeah, right,  
2 right.

3 PANEL MEMBER BLANC: I know that some of that has  
4 to do with coding. But in fact there are narratives for  
5 those case reports. And since we're talking about six in  
6 which -- six case reports in which there was pure  
7 endosulfan and not some mix, don't you think it would be  
8 worth it to go back, pull those reports, and actually  
9 summarize, since your entire human case literature  
10 otherwise is one report from India and one report from  
11 southeastern United States? I mean why have that  
12 elaborate pesticide illness reporting system if you --  
13 isn't this the ideal time you'd want to actually use the  
14 data?

15 And also in the "Human Section" on page 86,  
16 actually I think that's where it should go since it's the  
17 only -- some of the only human data you have, or you  
18 should refer back to it.

19 But the first paragraph there, I think there  
20 might have been a word processing error or something. Can  
21 you see where the report describes six patients?

22 DPR STAFF TOXICOLOGIST SILVA: Uh-huh.

23 PANEL MEMBER BLANC: There's no reference and I  
24 don't know what the report is.

25 DPR STAFF TOXICOLOGIST SILVA: Oh, I'm sorry. I

1 must have just -- yeah.

2 PANEL MEMBER BLANC: Is it possible that that's  
3 the Eli report from '67? It's not referenced anywhere. I  
4 mean there was an old report in literature, E-l-i, Charlie  
5 Hine was a coauthor.

6 DPR STAFF TOXICOLOGIST SILVA: Oh. That sort of  
7 rings a bell.

8 PANEL MEMBER BLANC: I think it got chopped off  
9 inadvertently or something at some point, and then the  
10 reference died with it.

11 DPR STAFF TOXICOLOGIST SILVA: There have been so  
12 many drafts of this thing that sometimes I wonder where  
13 things go.

14 Okay.

15 PANEL MEMBER BLANC: You might also want to take  
16 a quick look at Schaumburg and Spencer's second edition.  
17 Boy, there's a fairly erudite discussion of this class of  
18 pesticides. And some of their citations are not exactly  
19 journal articles. There are other texts which seem -- but  
20 based on the way they're citing them, they seem to be  
21 texts which actually have primary data in them or  
22 something. I can't really tell. That may not be the  
23 case. But you should look if you have that reference and  
24 just double check.

25 CHAIRPERSON FROINES: Their first book came out

1 about 1980. So this is one that came out in the latter  
2 '90s I think. So I wouldn't get confused because the old  
3 book has been around for a long time.

4 PANEL MEMBER BLANC: Right. But those were the  
5 things that confused me.

6 PANEL MEMBER BYUS: I have a few comments.

7 CHAIRPERSON FROINES: Please.

8 PANEL MEMBER BYUS: I agree with the tumor  
9 promotion. Under genotoxicity comments I had exactly the  
10 same thing. The data's not totally definitive but there's  
11 plenty of indication. So you really need to make a little  
12 more definitive statement about that.

13 I have one question about the pharmacology, your  
14 first slide or whatever is there on the first -- about the  
15 absorption.

16 No, keep going backwards.

17 That one.

18 And I kept reading it over and over in the --  
19 and, again, maybe I'm just not getting it. But generally  
20 if 75 percent -- if you go to the bottom -- by oral gavage  
21 shows up in the feces, that's indication of poor  
22 bio-availability, not a lot of absorption. I mean  
23 otherwise if 75 percent of what you missed are showing up  
24 in the feces, that's not a hundred percent absorption.  
25 Yet oral absorption, rat gavage, 87 percent, assume 100

1 percent. I kept reading it over and over again and I  
2 don't know what it is. So I don't understand.

3 DPR STAFF TOXICOLOGIST SILVA: Well, I think  
4 that --

5 PANEL MEMBER BYUS: I understand blocking off  
6 bile duct and looking and see what you got. That was  
7 good. But I don't get the -- to see what -- you know,  
8 you're getting enteropathic circulation.

9 DPR STAFF TOXICOLOGIST SILVA: Yeah, I think  
10 they're recovering total radioactivity rather than  
11 metabolites per se. So 13 percent of administered  
12 radioactivity's coming out in the urine and 75 percent in  
13 the feces.

14 PANEL MEMBER BYUS: So that if you increased the  
15 amount, then that process saturates and all of it gets  
16 absorbed. I don't know what the mechanism is. It just  
17 doesn't -- you know, it's just -- it doesn't make sense to  
18 me. I mean it might make sense. I mean it may really  
19 make sense.

20 So clear that up, would you, because it just --  
21 it just stands out as something being inconsistent  
22 completely.

23 DPR STAFF TOXICOLOGIST SILVA: Okay.

24 PANEL MEMBER BYUS: I have just a couple more  
25 comments, one about the reproductive toxicity. You know,

1 it actually seems like this is a fairly reproductively  
2 toxic compound, if you read it study after study. Test is  
3 spermatogenesis, all of the -- all kinds of -- now, again,  
4 these are occurring at higher doses than you're picking  
5 here, correct?

6 DPR STAFF TOXICOLOGIST SILVA: Right.

7 PANEL MEMBER BYUS: But still I mean when you  
8 conclude on page 67 in your summary, "Many studies  
9 obtained from the open literature showed direct effects on  
10 the male reproductive tract, although these effects did  
11 not alter reproductive performance," and I don't really  
12 know where that is. I mean there's some statements in  
13 here that -- sperm count in gavage deference was  
14 significantly decreased and their motility was sluggish.

15 DPR STAFF TOXICOLOGIST SILVA: Well, we're  
16 actually going to be revising that section, because I've  
17 put together all the pertinent studies and -- to show the  
18 studies, the duration, the author, the --

19 PANEL MEMBER BYUS: Okay. Because it says -- you  
20 know, you conclude there are no effects in the  
21 reproductive parameters for either sex. I mean I don't --  
22 it just seems inconsistent again to me.

23 DPR STAFF TOXICOLOGIST SILVA: Yeah. I'm going  
24 to get --

25 PANEL MEMBER BYUS: I mean after study after

1 study after study you list all these effects, every study  
2 is showing reproductive, particularly in the male.

3 DPR STAFF TOXICOLOGIST SILVA: But it's the dose  
4 and the route and --

5 PANEL MEMBER BYUS: But you should make some  
6 comment that at the doses used in these studies you're  
7 seeing that. But that, you know, at much lower doses that  
8 you might see with exposure, this is way, way above what  
9 you'd see. Something like that.

10 DPR STAFF TOXICOLOGIST SILVA: Yeah, I'm going to  
11 be -- no, I have another table and adding to the section  
12 or revising the section.

13 PANEL MEMBER BYUS: And then I do have --

14 CHAIRPERSON FROINES: Can I just comment just --

15 PANEL MEMBER BYUS: Oh, sure.

16 CHAIRPERSON FROINES: I would agree with the two  
17 of you about that, because obviously the estrogenic  
18 effects, the reproductive effects, all of this is emerging  
19 science. And my experience is that as the science  
20 emerges, you tend to get more, not less; hence, our view  
21 of lead compared to 50 years ago. And that I would  
22 actually put a paragraph in the document someplace that  
23 acknowledges the reproductive and endocrine effects as an  
24 emerging science to be taken seriously.

25 PANEL MEMBER BYUS: And of course stress the

1 dose, as you say. Because if these are all occurring at  
2 extremely high doses --

3 CHAIRPERSON FROINES: No, I think the endpoint  
4 that they chose is exactly the right one.

5 PANEL MEMBER BYUS: And then my last concern I  
6 have -- I just want to echo. The reported illnesses, the  
7 human data, struck me exactly the same way. I mean there  
8 must be narratives, I mean these several individuals who  
9 were exposed. I mean I have notes here like what  
10 concentrations were they exposed to? Was this the  
11 concentrate or was this the diluted form? You know, and  
12 what happened to them? I mean they died. One person  
13 died. And the other person had permanent --

14 PANEL MEMBER HAMMOND: Did you find that  
15 paragraph?

16 PANEL MEMBER BYUS: Right, exactly. I mean  
17 permanent paralysis, irreversible. I mean these kinds of  
18 things are, you know, very, very important, one would  
19 think.

20 So I mean you just need a little bit -- you know,  
21 in terms of the -- again, back to the toxicology, back to  
22 the dose, what was -- you know, even if you don't know  
23 exactly what the exposure was, you can get some --

24 PANEL MEMBER HAMMOND: What were they doing?

25 PANEL MEMBER BYUS: What were they doing? Sure.

1 I mean --

2 PANEL MEMBER HAMMOND: What was the time reentry  
3 in the field?

4 PANEL MEMBER BYUS: Exactly, time, that kind of  
5 thing. I mean all those things I think are really  
6 relevant to this toxicology for the extent that it exists.  
7 So I would do that as well.

8 CHAIRPERSON FROINES: Since I had mentioned that  
9 one study that you said you missed, I just wanted to  
10 comment that I went through all the reproductive and  
11 endocrine studies that I could find on this compound, and  
12 I checked your references. And Basically as far as I can  
13 tell, you got most, if not all, of them. So I think -- it  
14 isn't as though it's not there.

15 DPR STAFF TOXICOLOGIST SILVA: But it's not --  
16 you'd like it more concise, and it will be.

17 CHAIRPERSON FROINES: I'd like one paragraph that  
18 says, "This is emerging science that we need to follow up  
19 on over time."

20 PANEL MEMBER HAMMOND: Yeah, I would second that,  
21 because I think that there is that kind of interest in  
22 endocrine disrupters and in the reproductive effects. And  
23 who knows where it will go eventually. It's nice to at  
24 least have laid out what's known at this point. And you  
25 can conclude by saying it's not the most sensitive

1 endpoint, but that those effects are there. I think  
2 they're worthwhile --

3 PANEL MEMBER LANDOLPH: And, Marilyn, when you  
4 put those enzymes down that are thought to be involved in  
5 metabolism, if it's known what receptors they bind to and  
6 how they activate the metabolism, you know, maybe by  
7 binding to a receptor, translocation to the nucleus, new  
8 RNA, if that's known, if you could just sketch a couple  
9 sentences there, that would help out too.

10 PANEL MEMBER BYUS: My last comment was simply  
11 about the P-450 induction. I mean there must -- you  
12 mention it, it induces P-450. But does it -- do you know  
13 what isozymes it induces, those kinds -- I mean -- and,  
14 again, I'm not trying to just -- so based on evident --  
15 you know, the mechanism of action-based analysis for  
16 everything is very prevalent. And so this is -- I mean if  
17 you remember that this was the previous thing we were  
18 looking at, it's all laid out of which of the isozymes  
19 are -- again, it's very important.

20 DPR STAFF TOXICOLOGIST SILVA: Okay.

21 PANEL MEMBER BYUS: It's not trivial.

22 CHAIRPERSON FROINES: Can I disagree?

23 PANEL MEMBER BYUS: Oh, all right.

24 CHAIRPERSON FROINES: And I want to defend --

25 PANEL MEMBER GLANTZ: No.

1 (Laughter.)

2 CHAIRPERSON FROINES: -- the DPR folks,  
3 because --

4 PANEL MEMBER GLANTZ: He doesn't pay any  
5 attention to us.

6 CHAIRPERSON FROINES: What?

7 PANEL MEMBER GLANTZ: Nothing.

8 You said, "Can I disagree?" And we both said no.

9 (Laughter.)

10 PANEL MEMBER GLANTZ: And you just kept going  
11 anyway.

12 (Laughter.)

13 PANEL MEMBER GLANTZ: I know it was a rhetorical  
14 question.

15 CHAIRPERSON FROINES: I think that the  
16 document -- the strength of the document is that it  
17 gets -- it basically focuses on getting where they want to  
18 go, and I think that's a very good thing. Because I think  
19 that's what these documents should be about.

20 You two are basically wanting her to make this a  
21 literature review.

22 PANEL MEMBER BYUS: No.

23 PANEL MEMBER LANDOLPH: No.

24 CHAIRPERSON FROINES: And I think that you  
25 should -- I think if you want to put P-450 and which

1 isozymes are important, so on and so forth, I just think  
2 it should be limited and not ask her to do a whole thing  
3 on P-450 chemistry. I just don't think it's valuable.

4 PANEL MEMBER LANDOLPH: You can say it in a short  
5 paragraph.

6 DPR STAFF TOXICOLOGIST SILVA: Yeah, I have some  
7 good papers that --

8 PANEL MEMBER LANDOLPH: And if there's a review,  
9 just cite it and write three lines or four lines and  
10 that's it.

11 PANEL MEMBER BYUS: One sentence. In the  
12 sentence --

13 DPR STAFF TOXICOLOGIST SILVA: And I can add them  
14 to the --

15 PANEL MEMBER BYUS: Add it to the sentence.

16 DPR STAFF TOXICOLOGIST SILVA: -- the metabolism  
17 thing, yeah.

18 PANEL MEMBER BYUS: Right.

19 CHAIRPERSON FROINES: The hell with you two.

20 (Laughter.)

21 PANEL MEMBER GLANTZ: I was told to point out the  
22 previous statement was a joke for the record.

23 (Laughter.)

24 PANEL MEMBER BYUS: Please, put that down.

25 (Laughter.)

1 CHAIRPERSON FROINES: We have -- Paul's left.

2 We're down to four people plus -- five.

3 We're a quorum?

4 PANEL LIAISON BEHRMANN: Yes.

5 CHAIRPERSON FROINES: Now, shall we continue now

6 or shall we take it up next time?

7 PANEL MEMBER GLANTZ: Next time.

8 CHAIRPERSON FROINES: Next time.

9 PANEL MEMBER GLANTZ: I have one question. Are  
10 you going to do another draft of the document based on --

11 DPR STAFF TOXICOLOGIST SILVA: I sure am. Oh,  
12 yeah.

13 CHAIRPERSON FROINES: And we have --

14 PANEL MEMBER GLANTZ: Now, will we also for the  
15 next meeting have the public comments and the response to  
16 comments too?

17 Yes. Okay, good.

18 PANEL MEMBER HAMMOND: This is by the December  
19 meeting?

20 CHAIRPERSON FROINES: I would still argue  
21 to -- because given the tone of your voice, I would argue  
22 keep the rewrites limited and meaningful so we don't --  
23 all due respect to my two friends here, you know, that we  
24 keep it within confines.

25 PANEL MEMBER GLANTZ: And maybe use the famous

1 red line strike-out method so people can see -- you know,  
2 so you don't have to read everything again.

3 DPR STAFF TOXICOLOGIST SILVA: I see, yeah.

4 Are you -- I mean are we going to pursue the  
5 endocrine or are we going to -- I mean do you want --

6 CHAIRPERSON FROINES: I say, as far as I'm  
7 concerned, it should be a paragraph.

8 DPR STAFF TOXICOLOGIST SILVA: Okay.

9 CHAIRPERSON FROINES: A paragraph.

10 DPR STAFF TOXICOLOGIST SILVA: How about a table?

11 CHAIRPERSON FROINES: Whatever you -- that's  
12 right. A table that says here are studies and we'll look  
13 forward to emerging science. Just in a sense note that  
14 you're aware of this emerging field. And so when it comes  
15 up again in the future, and of course it's going to in  
16 some chemical or other, that we have it in the document.  
17 That was all I -- I wasn't trying -- I certainly don't  
18 think you should get into a whole discussion on endocrine  
19 disruption. I mean --

20 DPR STAFF TOXICOLOGIST SILVA: No, I prepared --

21 PANEL MEMBER BYUS: No, and my -- yeah, and my  
22 concern about that was not his concern that you talk about  
23 endocrine disruption. It just seems like you listed  
24 nicely all the endocrine effects and then sort of wrote  
25 them off. And the reason is is because of the dose, that

1 they're all occurring at very high doses. If that's the  
2 reason, that's all I would need in the summary, to say,  
3 yes, these things all occurred, but they occurred in  
4 animal models at very high doses that are tenfold or  
5 hundredfold -- whatever it is -- higher than these other  
6 effects.

7 So, you know, that's all I want to see.

8 CHAIRPERSON FROINES: But I would argue something  
9 different, which is interesting. Because as we move  
10 into -- as we move into what people are calling the new  
11 science, and we've lived through chronic animal bioassays  
12 and acute bioassays and Subphrenic bioassays since the  
13 seventies and eighties and even up to the present, but,  
14 you know, everybody's talking about new high through-put  
15 systems for doing short-term testing. And so the science  
16 may not be ready for prime time, but it's coming along.  
17 And at some point we're going to be making decisions about  
18 dose response, not based on an animal NOEL, but it's going  
19 to be based on some, you know, oxidative stress measure or  
20 NRF2 measure or what have you, and that's going to be a  
21 different -- there the dose situation's going to be quite  
22 different because it's going to be quite low. And so  
23 we're going to have to figure out how we're going to deal  
24 with that coming down the road.

25 So I think that just the issue of NOELs is

1 a science -- you know, it's from 1950.

2 PANEL MEMBER BYUS: I wouldn't argue with you,  
3 but --

4 CHAIRPERSON FROINES: Yeah. So I think it's --

5 PANEL MEMBER BYUS: -- we're always going to have  
6 to deal with the dose though. The dose is going to be the  
7 key issue no matter what the assay is. It's relative to  
8 exposure.

9 CHAIRPERSON FROINES: Yeah, but all I'm saying is  
10 that I think that ten years from now we'll be looking at  
11 things differently in terms of dose response.

12 PANEL MEMBER HAMMOND: I think that's all true.  
13 But I also think that it's important to at least lay out  
14 what are the categories of health effects that occur from  
15 something.

16 CHAIRPERSON FROINES; Yeah, of course.

17 PANEL MEMBER HAMMOND: And even if they're not  
18 the critical ones upon which you set the dose. Just so  
19 the people know that these are other -- the categories in  
20 the general things. But, again, it doesn't have to be a  
21 full 20-page section. What works best for you in how to  
22 present it. But I think just presenting that information  
23 is useful.

24 CHAIRPERSON FROINES: Are we --

25 DPR ASSISTANT DIRECTOR JONES: Let me just ask

1 one question of the panel.

2 Did it work previously on Methidathion when staff  
3 went back and took your ideas and thoughts and  
4 incorporated and we provided you an annotated highlighted  
5 copy that showed the changes and tried to summarize that?

6 Because we'll -- And, John, assuming that we will  
7 be discussing this in December 4th, that we'll get you a  
8 copy of that well in advance of the meeting and also  
9 provide you the comments and response to comments prior to  
10 that.

11 CHAIRPERSON FROINES: I don't think I'm overly  
12 optimistic to say that I think we can complete this  
13 document. And so one of the things we'll want to do  
14 perhaps, if it's okay with the Panel, is work on the  
15 findings between now and the next meeting as well. And  
16 then hopefully we can -- then we'll be in good shape.

17 (Laughter.)

18 PANEL MEMBER BYUS: With the comment that --

19 CHAIRPERSON FROINES: I can see why this  
20 document -- I can see why she would like this document to  
21 go away.

22 PANEL MEMBER BYUS: The comments are crucial. I  
23 mean as you know the Panel spends a lot of time reading  
24 and analyzing the comments. We take them very seriously.  
25 In fact, it is usually what I -- when I'm reading these

1 documents, what I read first. I know Stan taught me that  
2 many years ago, and I still do it. And I use the comments  
3 and then I read the document.

4 So they are very important and we really do  
5 listen to them and we really do consider them in depth.  
6 So they really are very important and it is nice to have  
7 them generally ahead of time before we have the document,  
8 because it sort of saves -- at least in the way I do it,  
9 it saves me some time and energy. But that's okay.

10 PANEL MEMBER GLANTZ: Yeah. Another thing  
11 related to that is this difference of opinion with OEHHA  
12 and how to handle exposure to children or infants, and how  
13 much of a correction factor to put in that. It would be  
14 nice if that got resolved. Or at least, if you can't come  
15 to an agreement, have the arguments on both sides laid out  
16 and then we'll decide what to do.

17 CHAIRPERSON FROINES: Well, I think it's -- I  
18 think it's internal. Yeah, I don't think we could in a  
19 sense define it.

20 Do we -- I want to delay us one minute longer.

21 I might like to borrow some of your slides for my  
22 risk assessment class. Those were really nice slides.

23 (Laughter.)

24 CHAIRPERSON FROINES: Can I get an adjournment.

25 PANEL MEMBER GLANTZ: I move we adjourn.

1 CHAIRPERSON FROINES: Second?

2 PANEL MEMBER BYUS: (Raised hand.)

3 CHAIRPERSON FROINES: All in favor?

4 (Hands raised.)

5 CHAIRPERSON FROINES: I would never stop using

6 Andy Salmon's slides, but those were good too.

7 (Thereupon the California Air Resources

8 Board, Scientific Review Panel adjourned

9 at 3:00 p.m.)

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## 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 4th day of October, 2007.

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