MEETING

STATE OF CALIFORNIA

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

PROPOSITION 65

DEVELOPMENTAL AND REPRODUCTIVE TOXICANT

IDENTIFICATION COMMITTEE

JOE SERNA JR.

CAL/EPA HEADQUARTERS BUILDING

1001 I STREET

COASTAL HEARING ROOM

SACRAMENTO, CALIFORNIA

WEDNESDAY, JULY 13, 2011

9:06 A.M.

JAMES F. PETERS, CSR, RPR
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APPEARANCES

COMMITTEE MEMBERS

Dorothy T. Burk, Chairperson, Ph.D.

Ellen B. Gold, Ph.D.

Carl Keen, Ph.D.

Hillary Klonoff-Cohen, Ph.D.

Linda G. Roberts, Ph.D.

La Donna White-Porter, M.D.

STAFF

Dr. George Alexeeff, Acting Director

Mr. Allan Hirsch, Chief Deputy Director

Ms. Carol Monahan-Cummings, Chief Counsel

Dr. Jim Donald, Chief, Reproductive Toxicology and Epidemiology Section

Ms. Cynthia Oshita, Proposition 65 Implementation

Dr. Lauren Zeise, Chief, Reproductive and Cancer Hazard Assessment Branch

ALSO PRESENT

Dr. Jay Murray

Dr. Artie Lawyer, Technology Sciences Group

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PROCEEDINGS

CHAIRPERSON BURK: Good morning, everyone, the hearty people that are here bright and early.

We'll continue the meeting we started yesterday. And we are now on Agenda Item number 5, Prioritization of Chemicals for Future Developmental and Reproductive Toxicant Identification Committee Review. And we'll begin with staff presentations. Looks like Jim Donald.

(Thereupon an overhead presentation was Presented as follows.)

DR. DONALD: Good morning. My name is Jim Donald, and I'm going to briefly run through how we prioritize the five chemicals that were sent to the Committee for which compilations of relevant abstracts were sent to the Committee.

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DR. DONALD: So this is just to refresh everyone's memory. This flow chart shows the various steps we follow in our prioritization process. The next couple of slides will briefly review the screens that were discussed with and recommended by the Committee in its last meeting. And then I'll discuss how we applied those screens and what the outcome was.

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DR. DONALD: So our starting point for this round

of prioritization was the same tracking database as we used previously. And from that, we identified chemicals that past the initial screens as having some -- excuse me, passed the initial screens for the availability of some relevant toxicity data, and for some potential for exposure in California.

And for this round of prioritization, the tracking database has been updated with a substantial number of additional chemicals that came to our attention since the last round of prioritization.

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DR. DONALD: So using these screens that were recommended by the Committee at the last meeting, we attempted to identify chemicals that are known to occur in humans, and also have a substantial amount of relevant toxicological data from animal studies.

Our specific goal was to identify important candidates of direct relevance to humans. Since most of our staff are toxicologists who deal primarily with animal data, focusing on the animal data in this round of prioritization also was intended to identify candidates that would allow us to use our staff resources more efficiently, since we would not be dealing only with chemicals that had predominantly epidemiologic data.

And as I mentioned at the last meeting, we do

anticipate using the screen for chemicals that have relevant epidemiologic data in humans, again, at some point in the future.

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DR. DONALD: For the exposure screen, we proposed to begin by reviewing data from compiled sources, such as the National Health And Nutrition Examination Survey to identify chemicals that had actually been detected in humans. Depending on how extensive those data were, we also said that we would move on, if necessary, to the open literature.

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DR. DONALD: For toxicity data, we propose to identify the relevant studies of apical endpoints of developmental and reproductive toxicity, then chose a cutoff number of studies that would yield approximately eight to 15 candidate chemicals.

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DR. DONALD: More than a thousand chemicals were screened for relevant DART data by searching in TOXNET using an extensive list of relevant key words. TOXNET is a service of the National Library of Medicine that allows searches to be conducted simultaneously on a range of databases on toxicology, hazardous chemicals, environmental health and toxic releases. About 730

chemicals were found to have evidence of developmental or reproductive toxicity.

About 175 of those chemicals had 30 or more references that appeared in TOXNET. Those 175 or so chemicals were then compared to the chemicals identified in NHANES as having been found in human samples. There were about 133 chemicals that had both 30 or more DART citations and also appeared in NHANES. So we did not feel it was necessary to use any additional sources of biomonitoring information or -- excuse me, any additional sources of biomonitoring data.

When these chemicals were ordered according to the number of citations from TOXNET, we found that 19 chemicals had 60 or more citations.

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DR. DONALD: This table shows the 19 chemicals for which we found 60 or more citations in TOXNET. We decided not to proceed any further with the three chemicals highlighted in the table. The two chemicals highlighted in yellow, cotinine and mono-2-ethylhexyl phthalate are metabolites of the listed chemicals nicotine and di-2-ethylhexyl phthalate respectively. And most, if not all, of the exposure to these chemicals occurs via exposure to the listed parent chemical.

The chemical highlighted in green, genistein, you

heard about yesterday. It's included in an ongoing evaluation of soy infant formula by the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction, which of course is still an the authoritative body under Proposition 65.

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DR. DONALD: So as I mentioned earlier, we had decided that we needed to establish a criterion for the number of reports of DART endpoints that would be a basis for chemicals going forward. We actually decided to employ two criteria. One was that there was a total of 15 or more reports of relevant DART endpoints of any type. And the second criterion was that there was a total of 10 or more reports of any single relevant DART endpoint, by which we mean 10 reports of developmental toxicity or 10 reports of female or male reproductive toxicity.

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DR. DONALD: The eight chemicals above the black line in this table met one or more of the criteria we established. For three of the chemicals, after compiling the information relevant to prioritization, we decided not to proceed any further.

In the case of platinum, which is highlighted in pink in the table, all of the relevant studies were of chemotherapeutic drugs that contained platinum. It seemed

unlikely that the contribution of platinum to the effects of the drugs could be determined. The two chemicals highlighted in green naphthalene and styrene were the subject of recent evaluations by authoritative bodies that did not lead to formal identification of developmental or reproductive toxicity.

As noted in our 2004 prioritization procedure document, chemicals are generally not proposed for DART IC review that have been recently reviewed by an authoritative body and found to have insufficient evidence of reproductive toxicity. An exception to this may be if compelling new data have become available since the evaluation.

For both of these chemicals, we determined that there had been no substantial addition to the relevant literature since the authoritative body evaluations were conducted.

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DR. DONALD: So for the remaining five of the chemicals benzo(a)pyrene, uranium, methyl parathion, deltamethrin, and xylene, the relevant abstracts or titles of studies were compiled and provided to the Committee in advance of this meeting to serve as a basis for discussion and recommendation by the Committee of chemicals for which hazard identification materials should

be prepared.

It should be noted that these compilations are intended to indicate the extent of the available data, but the complete studies have not been evaluated at this stage in the process. If a chemical is selected as a candidate for consideration for listing, the complete studies will be evaluated when hazard identification materials are prepared.

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DR. DONALD: And at this point, I'd be happy to take any questions that you have.

CHAIRPERSON BURK: I guess I see no questions. So as I understand it, the Committee will discuss each of these and determine, one by one, whether or not we feel that it -- that we would like to see the development of hazard identification materials on that chemical, if we think there is enough there or whatever. So we will do that.

First, there's time for public comments here in the agenda. I just wanted to know if anyone wanted to make a comment, otherwise we'll just get started. And as far as I'm concerned, we're going to do these one by one. So if there are public comments on a particular one, we can take them at that time.

Also, it's my understanding that Linda will

recuse herself from xylene -- oh, something else.

COMMITTEE MEMBER ROBERTS: Benzo(a)pyrene.

CHAIRPERSON BURK: And benzo(a)pyrene. So we'll take five votes, whether there's five people or six people, is that correct, Carol?

CHIEF COUNSEL MONAHAN-CUMMINGS: Well, this is advice, so you don't have to have a particular number. You're just giving us advice.

CHAIRPERSON BURK: Okay. That's fair. Good. I don't like voting.

ACTING DIRECTOR ALEXEEFF: Yeah. If I can make one comment. You don't have to have a particular vote, but it would be good to get a sense if there's a recommendation how much of the Committee, you know, feels strongly about it.

CHAIRPERSON BURK: Yeah. We'll see if there's a consensus or not. That shouldn't be too difficult.

So let's start with Benzo(a)pyrene. And I have to find my notes.

Did anyone have a good system for this?

(Laughter.)

CHAIRPERSON BURK: I'm looking at Dr. Gold. Actually, I'll tell you what I did, and then tell me what you -- I mean, I went through all of them, and I wanted to see, since it's mostly animal data, you know,

how many of the sort of traditional type of studies with multiple dose levels and, you know, that kind of thing, how many of the studies appear to be more mechanism type of studies, sometimes seemingly by not the relevant route or whatever. But anyway, just to get a sense of whether when we go to look at it whether there will be enough of the kind of information that we're looking for.

So again, since they're only abstracts, you don't always know what the actual study is going to say. So we're not making a judgment now on whether it be listed our not, but just whether or not we should proceed.

So I'll let you give me -- why don't you take the first one and give us your thoughts.

COMMITTEE MEMBER GOLD: Well, first of all, let me say, I wasn't as systematic about this as I was with yesterday's activities.

I did sort of just go through -- the ones that seemed mechanistic, I didn't -- I just noted that that was the case. The ones that had findings -- I'm sorry. It's on.

So the ones that were mechanistic, I just kind of noted -- made a mental note of that, but the ones that seemed to have findings, I kind of -- I went through made a note as to whether they were positive or negative. I didn't really try to do any evaluation of the quality of

the studies or anything like that, just to get a sense of whether there seem to be enough evidence there to suggest that, you know, further evaluation should be done. So that's kind of how I did that.

And I didn't really quantify anything like I did yesterday. So I'm not sure I'm going to be the most helpful person to you.

I do have one question, however, which is we have five compounds that we're considering. Do they want a ranking of those or just an indication of each one, whether --

CHAIRPERSON BURK: I was asked to have an up or down on each one, but I think if you feel that there's one, in particular, that, you know, really strikes you should be first, we'll offer that advice.

Does anyone want to comment on benzo(a)pyrene? It certainly had a lot of studies at least for development.

What I noticed is that some of the endpoints were sort of interesting for development. Immunodeficiency seemed to be a big one. And there was some neurobehavioral toxicity, and then some male effects.

COMMITTEE MEMBER WHITE-PORTER: I think with a couple of things. I wrote down five endpoints that kind of struck me. Brain development -- the impairment of

brain development, along with the possibility of intradermal and cranial hemorrhage. Those kind of stuck out for me, as well as fetal immunity, and also the impairment of fetal immunity, and neurotoxicity. Those were sort of the five endpoints that really struck me initially with this particular chemical.

COMMITTEE MEMBER KLONOFF-COHEN: I had a quick question. So when I looked at the studies, there were five developmental studies that looked interesting. And I had a question in terms of, so if you find an interaction with what you're looking at and environmental tobacco smoke, like we did in one of the developmental studies, and then out of the two female reproductive studies the same thing, when there's a cigarette smoke involved with it, does that, in any way, complicate the findings for...

DR. DONALD: It would certainly complicate the findings.

Would it prevent identification benzo(a)pyrene?

COMMITTEE MEMBER KLONOFF-COHEN: Yeah.

DR. DONALD: We really couldn't say that until we had looked in detail at the studies, and, you know, looked at the study design, the analyses, and determine -- or ultimately you would determine if it came before you, whether or not you could distinguish the contribution of benzo(a)pyrene to whatever effect actually occurred.

COMMITTEE MEMBER KLONOFF-COHEN: Okay. Thank you.

COMMITTEE MEMBER KEEN: I can't help but observe we spent four hours yesterday talking about a compound that is in that precise class. I mean, sulfur dioxide -- all the data had other pollutants associated with it for the human studies. So I think that's -- there's our answer.

COMMITTEE MEMBER KLONOFF-COHEN: Well, since you said that, Carl, I mean, I know that the five developmental studies and the two female reproductive studies and two male studies, but there's 37 animal studies.

COMMITTEE MEMBER KEEN: But that was again, déjà vu of yesterday where --

COMMITTEE MEMBER KLONOFF-COHEN: I was wondering are you familiar with any of the animal studies. Like, do you have a sense in terms of how strong those studies are?

COMMITTEE MEMBER KEEN: My opinion is, as I did my internal ranking and I did have this one listed as number one. I'll make that observation.

COMMITTEE MEMBER KLONOFF-COHEN: Excellent. Okay. Great.

COMMITTEE MEMBER KEEN: I took some time and read some of the studies for each of these abstracts just to

get a sense of their relative strength.

COMMITTEE MEMBER KLONOFF-COHEN: Perfect. Okay. Great.

COMMITTEE MEMBER KEEN: But this one is high on my list.

COMMITTEE MEMBER KLONOFF-COHEN: Okay.

CHAIRPERSON BURK: I agree as well. So I'm taking that there's a fair consensus that we would want to proceed with benzo(a)pyrene.

Let's move to the next one, which is -- let me make sure I have the right one. I have deltamethrin, deltamethrin an insecticide, used to eradicate external parasites on farm animals, possibly getting into the food. I noted there are no human studies on anything. So this is strictly animal for any of the endpoints.

Just from glancing at the traditional sort of teratology experiments, it didn't appear to be a selective teratogen from this. It seemed like maybe with toxicity, but there were quite a few neurobehavioral studies. And I thought the male reproductive part looked potentially stronger.

Any other comments on it?

How did you rank this one, Dr. Keen.

COMMITTEE MEMBER KEEN: I was just going to say I concur with your analysis. I actually had this one ranked

last. That doesn't imply it shouldn't be looked at, but I wouldn't do it with a sense of great urgency.

CHAIRPERSON BURK: Okay. All right. Do others say up for this one? In other words, yeah, it shouldn't be maybe the highest on the priority, but it appears that there's enough sufficient data that we can at least make a decision on it.

COMMITTEE MEMBER ROBERTS: I would -- since I can chime in on this one.

CHAIRPERSON BURK: Okay. Please do.

COMMITTEE MEMBER ROBERTS: I can say that although some of the developmental work is not, say, the traditional teratology endpoints, they do indicate in the abstracts that they are dose responsive, which is a traditional way of looking at toxicology studies, which would strengthen it. So it looked to me like it had sufficient information for wherever it comes up in the ranking. And this is more thoroughly evaluated.

So I think there's enough of a case for us to take a look at, and not make a decision because we didn't have enough information. I think there is enough here.

CHAIRPERSON BURK: So there's enough information, yes.

All right. The next one is methyl parathion, which is acetylcholinesterase inhibitor insecticide. And

does anyone want to comment on this one?

COMMITTEE MEMBER KLONOFF-COHEN: Well, it's the same thing where we've got the two male reproductive studies that look okay, but it's just a question of what the 21 animal studies are.

CHAIRPERSON BURK: I thought the male looked the strongest potentially in terms of having --

COMMITTEE MEMBER KLONOFF-COHEN: Yeah, exactly.

CHAIRPERSON BURK: One thing I did notice in the male is that quite a few of those studies were from the same lab if you actually went through. Not that that matters. It's obviously their interest. But by the time I got to -- one of them I had written down, this is the same lab as five others before it. You know, so that doesn't necessarily mean anything. I just noted that.

And then I don't remember. I put what to make of the one mating study, but at least there is one mating study. So where did you rank this one, Dr. Keen. I'm curious.

COMMITTEE MEMBER KEEN: Well now, I'm going to throw a curve, because I ranked this one and uranium as being about equivalent. And so I had them, if you will, kind of that two, three category. And where I was struggling a bit and trying to filter out which one would I think be higher on the priority is -- would be based on

information which I don't think we have. That is what is the potential proportion of the population or the impact of what we're looking at, because if I think I had that, I'm probably going to wind up leaning towards -- I'm speaking a bit out of turn here, but since this is a general discussion, uranium ahead of it, because where I look at the --

CHAIRPERSON BURK: Really. I kept asking how many people are exposed to uranium?

COMMITTEE MEMBER KEEN: Well, in terms of non-radioactive uranium, the current EPA limits some people have debated that there maybe should be lowered, and there's some evidence for that.

But again, that's -- only because I happen to have read that literature did I say, "Oh, I think this could be really hitting a lot of people". I don't have the same information here, and I'm embarrassed to say I didn't take the extra time to try to sort out what the total exposure -- you know, potential for population exposure is. So the long answer to your simple question.

CHAIRPERSON BURK: No, but we know there is exposure, because that was part of the screen. I mean, it's not necessarily our job to figure out how much, but I know it weighs into the decision about prioritizing.

COMMITTEE MEMBER KEEN: Since it's ranking, yeah.

I think it clearly is deserving of additional study, but how to exactly rank it.

CHAIRPERSON BURK: Well, I was confused. So maybe someone on the staff could, since now we're on uranium, explain to me if it's equivalent to study the depleted uranium, and the enriched uranium, and then the uranyl acetate dihydrate. I mean, are those all considered equivalent, if we were to list uranium?

DR. DONALD: It would potentially depend on exactly how the listing was made, if you listed uranium and uranium salts or uranium and uranium compounds, it would capture uranyl acetate.

We have some listings. For example, the listing for lead has been interpreted to capture lead compounds. And that was done very early on as Dr. Burk well knows. And subsequent listings, we've tried to learn from the problems that have arisen from earlier listings. So we've tried to be as clear as possible in the more recent listings as to what is captured by the listings.

So if uranium came before the Committee, it would probably be your prerogative to determine if the listing was for some particular forms of uranium, for all uranium compounds or possibly even just for the metal.

CHAIRPERSON BURK: I just wonder if it would make it tricky, because there wouldn't be as many studies. You

know, if we had to look at each one of those different aspects of it.

DR. DONALD: If I could add. If we do end up bringing uranium before you, we would try and make it clear, you know, what the evidence was for each form of uranium and hopefully inform your decision in that way.

COMMITTEE MEMBER KEEN: Yeah. I think that would be essential, because the work I'm familiar with is uranium unfortunately has a nasty habit of interfering with some very specific enzymes, and it is driven by the form of the uranium and the salt complex of it. So it isn't very straightforward, which would make it perhaps fun, but also a real challenge.

CHAIRPERSON BURK: So just to catch up, do we have a general consensus so far on uranium too as well as methyl parathion?

Okay. And then finally the last one is xylene, a solvent. And I know that we already have listed benzene and toluene, I think, because I remember those from the past. I don't know why we never got to xylene in the past. Was it lack of information or what?

DR. DONALD: Xylene has come up in the past under other forms of prioritization. It just never made it to the head of the queue before we switched to a different form of prioritization.

CHAIRPERSON BURK: Now, the main thing I noted there wasn't a whole lot for male or female. And there was a, what seemed like a nice study in development that was negative. But that doesn't matter, it's there. And a lot by the Hass Lab, which seemed to be the same thing. In other words, they were using 500 parts per million technical xylene, and doing various behavioral -- neurobehavioral tests.

I don't know. What's your feeling on xylene? I guess we're not judging it. We're saying is there enough information that we think they should go ahead and --

COMMITTEE MEMBER KLONOFF-COHEN: There's the study on -- let's see. So there was a study on spontaneous abortion where the odds ratio was a 3.1. And that was significant.

CHAIRPERSON BURK: So there is Epi, which is nice to add to it.

COMMITTEE MEMBER KLONOFF-COHEN: Yeah. There's one where there's a shorter length of luteal phase, and it decrease of luteal progesterone levels. There was one on --

ACTING DIRECTOR ALEXEEFF: Can you get a little closer.

COMMITTEE MEMBER KLONOFF-COHEN: Oh, sorry -- one on spontaneous abortions.

In terms of her -- so those are okay. The one for the male was a combination of exposure to the benzene, toluene, and xylene affected the sperm. And then there are 13 animal studies.

CHAIRPERSON BURK: Well, it's nice to have some Epi studies mixed in with the animal studies.

What's the feeling of the group, yea or nay? Well, it couldn't have been your lowest ranked, Carl, because you already had that.

COMMITTEE MEMBER KEEN: It wasn't. I had it number four. But, you know, again, worthy of studying, absolutely. But there's limited resources, it just wasn't in the top few, in my opinion.

CHAIRPERSON BURK: All right. That's reasonable. So is that information helpful to you?

DR. DONALD: Yes, very helpful. Thank you.

CHAIRPERSON BURK: Okay. Are there any public comments at this point I should ask?

There's only two public in the whole audience.

(Laughter.)

CHAIRPERSON BURK: It's so quiet.

All right. So we'll proceed to Agenda Item 6, Update of the list of chemicals which have not been adequately tested as required presented by Carol Monahan-Cummings.

CHIEF COUNSEL MONAHAN-CUMMINGS: Good morning.

(Thereupon an overhead presentation was Presented as follows.

CHIEF COUNSEL MONAHAN-CUMMINGS: As you may recall, from a couple meetings ago, there's a somewhat obscure provision of Prop 65 that really doesn't relate to the rest of the law that requires the State's qualified experts to decide whether or not they think a chemical has had sufficient study as required by federal and State law.

So what we have done for you, as we have in the past, is we requested information from U.S. EPA and also from the California Department of Pesticide Regulation regarding the chemicals that are currently on that list as not having enough data, and also asking whether or not there should be additional chemicals added to that list.

This year, we are actually only asking you to remove chemicals. I believe there's nine chemicals that U.S. EPA has advised us they have the sufficient data in on those now.

So essentially all we're asking you to do is advise us to go ahead and update the 27000 list. It's just kind of an anomaly. We'd like to do that ourselves, but we can't, because the statute says you do it.

Do you have any questions?

CHAIRPERSON BURK: Do you want us to vote?

CHIEF COUNSEL MONAHAN-CUMMINGS: Sure. The vote would be whether or not to remove these seven chemicals from the list.

CHAIRPERSON BURK: Okay. All those in favor of removing these -- I think it's nine chemicals -- two, four, six, eight -- nine chemicals from the list raise your hand?

All those in favor?

(Hands raised.)

CHIEF COUNSEL MONAHAN-CUMMINGS: Thank you.

CHAIRPERSON BURK: I think that's it.

All right. Agenda Item number 7, and Cynthia Oshita is coming forward for the first, chemical listings and safe harbor level development.

MS. OSHITA: Yes. Okay. Since the Committee met last October, OEHHA has administratively added, by mechanisms that were presented to you in the discussions yesterday, 18 chemicals. Two were listed as known to cause reproductive toxicity, and 16 were listed as known to cause cancer. And a summary table of these additions are in your meeting materials under the staff updates tab.

There are yet some other chemicals that are under consideration for administrative listing. And as was mentioned yesterday, we are considering listing methanol and BPA as causing reproductive toxicity. And then we are

also considering cocamide diethanolamine, tetraconazole, and kresoxim-methyl as being considered for listing for causing cancer.

Methanol is in the notice of intent to list phase. While all the others are in the data call-in phase. Comments have been received on each of these chemicals and they are under review.

In addition, OEHHA has announced the proposed administrative listing of yet some other chemicals, which include hydrogen cyanide and cyanide salts, which are under consideration for causing reproductive toxicity. And the public comment period will close on August 3rd, 2011.

Alpha methylstyrene, which is proposed for listing as causing reproductive toxicity and titanium dioxide is proposed for listing for causing cancer. No comments were received for alpha methylstyrene. And so we expect to include it on the next publication of the Proposition 65 list. Several comments were received for titanium dioxide and those are under review.

Also since last October, we have adopted Maximum Allowable Dose Levels, MADLs, for acrylamide and hexavalent chromium. The acrylamide MADL became effective April 29, 2011. And the hexavalent chromium MADL was recently approved by the Office of Administrative Law and

will become effective on July 29, 2011.

We've also proposed to adopt a MADL for avermectin. No comments were received on the avermectin MADL during the public comment period. And so its rule-making package will be finalized for submission to the Office of Administrative Law for approval in the very near future.

And lastly, we've also adopted two No Significant Risk Levels. One was for glycidol, and the other was for 2,4,6-trinitrotoluene. And these levels became effective February 25th, 2011.

Thank you.

CHAIRPERSON BURK: Thank you. Any questions of Cynthia?

Well done.

Next, we have a staff update on Proposition 65 litigation.

CHIEF COUNSEL MONAHAN-CUMMINGS: Good morning again.

CHAIRPERSON BURK: Carol Monahan-Cummings.

CHIEF COUNSEL MONAHAN-CUMMINGS: Just a reminder when Cindy was speaking about any of these chemicals that we talked about as in process, your group is -- or individuals are encouraged to make comments if you feel you should or need to on those listings prior to them

being final. So that's what we were talking about yesterday that you do have the ability to provide us input.

In terms of the litigation, we had four cases pending till very recently that were against OEHHA or the agency and the Governor as well.

One of them was the Chamber of Commerce versus OEHHA. Actually, it's the Chamber of Commerce versus Brown, I'm sorry. And in that case, we were -- the Chamber of Commerce sued to determine whether or not we had the authority to list chemicals under what's called the Labor Code listing mechanism. If you recall from yesterday, I mentioned that, that it -- you know, we list chemicals that are included on other lists, mostly occupational related, either -- that are under federal regulation primarily.

And in that case, we were successful at the trial court, and we were also successful at the court of appeal. And the Chamber has decided not to request review from the State Supreme Court, so that case is final now.

The other case that's pending in the court of appeal is the case that was brought by the Styrene Information and Research Council, and that has to do again with the Labor Code listings. And they're questioning is more narrow than the one that was decided in Chamber of

Commerce case. It has to do with the level of evidence that needs to be available before we can list a chemical.

That one has been pending in the court of appeal for over a year, and we have no idea when it's going to be heard.

The other older case is the Sierra Club versus Brown. And that was filed in 2007 and still pending in the trial court in Alameda. We've made a little bit of progress in that, in terms of some discovery stuff, but -- and we have kind of taken a little hiatus to try and work on settling the case, but haven't made a lot of progress in that regard. Your sister Committee, the CIC, are defendants in that case, along with our office, the Secretary and the Governor.

And it has to do with the listings from three of the methods we've talked about, the CIC listings and prioritization, which would include this group, the Labor Code and the authoritative bodies listings. And so those can all -- I mean, those are -- can all kind of touch this group. But for the most part, you guys aren't involved and are fortunately not named in that lawsuit.

The last one I wanted to mention is a more recent one where we were -- OEHHA was sued by a number of food industry groups over the recent listing of 4-MEI, which Cindy mentioned to you. It's actually a contaminant in

caramel coloring, and is used extensively by the food industry as well as others.

And we listed the chemical recently, and then we were immediately sued by this group. There's a hearing here in Sacramento on their lawsuit this Friday -- it's a busy week -- Friday morning. And we'll find out probably shortly thereafter what the decision of the trial court is. It doesn't take very long for the trial court to get through these, because it's basically, you know, you file your briefs, you have an argument, and then they decide. And so depending on the outcome of that, most likely it will go up on appeal.

As of this moment, that's all of the cases that we're aware of that are pending against our office. And I'd be happy to answer any questions that you might have.

COMMITTEE MEMBER ROBERTS: Carol, what was the name of the last chemical in the lawsuit?

CHIEF COUNSEL MONAHAN-CUMMINGS: 4-MEI. It's 4-methylimidazole.

CHAIRPERSON BURK: Public comment?

Jay Murray.

DR. MURRAY: Jay Murray. Here on my own behalf. And I just wanted to add one thing to what Carol said, especially since someone asked what the chemical was. 4-MEI is formed in a lot of food products. And it's

another one of these chemicals like acrylamide that's caused when you heat foods. It's a different set of naturally occurring substances in foods that can do it, but it's in a lot of different foods from -- because its present in certain types of caramel coloring. Caramel coloring is in a lot of foods. It's also probably formed in a number of goods that contain sugar when you heat the sugar.

CHAIRPERSON BURK: Thank you.

Yes. In addition to staff updates was a discussion about writing the reports, the hazard identification materials. Were you going to talk about that?

ACTING DIRECTOR ALEXEEFF: Yeah, I can start.

CHAIRPERSON BURK: George Alexeeff.

ACTING DIRECTOR ALEXEEFF: Yeah. First of all, I just want to thank the Panel for assisting us over time, in terms of trying to use resources as effectively as possible to provide whatever information might be needed to make a decision to move forward one way or the other. And the prioritization is a good example of that, where it came with a procedure, we did some, and then we came back saying, well, it would be great if we could try a slightly different procedure to balance the resources in terms of epi and toxicology, in terms of our staff resources, and

you assisted us on that.

We came forward with these chemicals recently, and you gave us some response on that. And over time, we've also been trying to revise or sort of tweak the hazard identification materials, so that the Panel receives the information it needs for a decision, but, you know, sort of also maximizes our resources.

So we thought it would be helpful to talk a little bit about preparing the materials and providing them to you, and to us, what might be some additional efficiencies that we could utilize, if you thought it would be okay, let's say, or maybe we could just talk about how that might work.

And, in particular, just for example, there were, you know, the chemicals that we just considered now. We will now proceed and look further into the chemicals and probably begin to write-up benzo(a)pyrene or begin the process for benzo(a)pyrene, and maybe one or two of the others.

And in that process, we may find out that although it looked like they are a lot of good studies. In the end, maybe there weren't very many good studies, or I think as -- I forget which chemical it was, but there was one chemical where I think it was noted there were a lot of developmental studies. Well, maybe there really

aren't any female or male reproductive studies.

So the question is how could we expedite preparing the materials so that we don't use resources trying to put together sort of a story that of which there's not much story. So that's -- I thought maybe the staff could talk a little bit about that.

DR. DONALD: Okay.

(Laughter.)

DR. DONALD: I don't have anything prepared for this. So extemporaneous.

As I'm sure the Committee members noticed, we did attempt some alterations or some refinements of the way that we presented material in the past for the current chemical that you considered yesterday.

We recognize that we often give you a great deal of material to go through in a relatively short period of time. So our concept at this time was to try and create something of a hierarchy of information. We provided summaries, fairly detailed summaries, but summaries nonetheless as the first level of information, summaries that integrated the information rather than summarized the individual studies. The summaries of the individual studies were presented as appendices this time to allow you to go to them as you needed to to understand the information.

And then the third level of information, taking advantage of the new technological advances that have occurred. We were able to give you all of the relevant material in electronic form to make it both accessible and hopefully easily searchable.

So we also tried to focus this time around a little bit more on the studies that appeared to be most informative, both in terms of the nature of their design, and the study outcome, the quality of the studies. Of course, there was a certain group subjectivity in that. And it's not our intent to bias the Committee in any way. We simply want to make the information as clear and accessible to you as we can.

But one thing we did, as we've always done in the past, is tried to be comprehensive in the material we provided. So one issue George is raising is for sulfur dioxide it was clear that the information on female reproductive toxicity was far less extensive than the information on other endpoints. And one question would be in the future if -- would you want to employ some sort of cut-off where the extent of information on a particular endpoint is below that cutoff, we wouldn't present that information at all. And if that's the case, what would the cutoff be? That would be one question.

Conversely, would you prefer us to continue as we

do now in trying to provide you with all of the relevant information, and all of the endpoints? And if so, is there a better way for us to do that, a way that would be more useful to you and more efficient for you?

DR. ZEISE: And just to add a little bit to that, I guess in addition to a cutoff, staff could use their judgment in looking at the evidence. And if it just didn't seem to quite be there, as we began the review, we wouldn't necessarily write-up all of those studies and cover that endpoint. That would be another option.

CHAIRPERSON BURK: I think I could see where there's, you know, one study on female, you could put the abstract, like we have. You could potentially have it on a CD, but not spend a lot of time bothering to, you know, analyze it or describe -- I don't know. You know, that would be fine with me, but I'm kind of curious how the others feel.

DR. DONALD: If I could just add one more point though. Your own criteria state that in some circumstances one study may be sufficient for listing.

CHAIRPERSON BURK: I know. That's why I wouldn't want you to skip it all together. That's why I would want there to be something there, so that we know, at least, that there are studies.

But if it were something, you know, where it was

one study and it was say a mixture that you couldn't figure out the contribution of the chemical of interest, it would be worth seeing it there, because it might fit into the big picture. But I don't think you would spend a lot of time, you know, giving us all the details. I don't know though. That's a tough one. That's a tough one to a. --

COMMITTEE MEMBER KLONOFF-COHEN: I just wanted to say that I though that this time particularly everybody did an amazing job in terms of the review. There were just so many studies. I thought it was really comprehensive, really -- I loved the tables and how you could get into the details of the studies. I really thought it was great.

So I guess my own -- I had a question in terms of is it because of the fact that in terms of just -- there's just so many hours in the day, it just would be easier and more efficient to make that decision? Because for me for the sulfur dioxide it was great to actually see the whole realm in terms if you're male and female and developmental and how that study or that area actually, you know, didn't necessarily have information at this time, so -- but is it more of a time issue or --

DR. DONALD: That's certainly a component. You know, we'd like the Committee to be able to consider as

many important chemicals as possible in any given time frame. The more time that and resources it takes us to prepare the materials, then obviously the fewer chemicals we can bring before you.

So there's sort of a balance. We want to keep feeding you relevant information, but we don't want to spend a lot of time preparing information that ultimately doesn't contribute to the listing decision.

COMMITTEE MEMBER KEEN: Just a modest concern I would have though, is sometimes, yes, there may be a very limited base of information, and it may not be overwhelmingly convincing, but it may be critical when it comes to considering biological plausibility.

If I had to find a fault, I think we have spent actually very little time on what is probably one of the most essential of the Hill criteria, that there needs to be not just a lot of associations and fingers pointing the right direction, but there's supposed to be biological plausibility.

And often times I think we're not giving a whole lot of attention to that. So I think if the decision is made, which would be appropriate if you look at a paper and say, well, there really -- it doesn't have much substance here, it could have -- it could be lacking controls. We could come up with multiple reasons, where

you're not going to weigh the date too closely, but if it argues against the mechanisms, which are potentially we're seizing on for another form of toxicity, I think it's important that we're alerted to that.

And maybe just even having the very -- the reference they're saying, not included because of lack of control or something of that nature. But that would be my biggest concern. We all know that there is a publication bias. And the publication bias is for finding somebody positive, in the case of reproductive toxicants, negative. And it's those neutral papers which tend not to surface.

And yet, if they're testing at what -- you know, again the plausibility issue, they become quite important for other reasons. So I just would urge the obvious caution about that.

COMMITTEE MEMBER GOLD: So I'd be a little bit nervous about a cutoff, that implies to me that -- like if there were only one or two studies, that you would want to have a certain critical mass of studies. But to me, if you have one really good study, I would like that to be included.

And some of the things in your potential list, not the ones that we talked about today, might even have, for example, a clinical trial, which, you know, we regard as sort of the highest quality study you could have. So

for example -- well, and I won't give examples, but that might happen.

And if there were a large enough clinical trial that was well conducted, even though it was only one study, I'd like to see it. So I would be hesitant to make a cutoff.

DR. DONALD: So it sounds like there's a sentiment among the Committee that we should continue to be comprehensive in what we include, but perhaps adjust the amount of information we provide based on the value that we think it would have to the Committee. So we might identify studies, and as Dr. Keen suggests, perhaps give a very brief reason for why they weren't discussed in detail, but still provide the study itself to the Committee, so that if you had an interest in it, you would have the opportunity to read the entire materials.

COMMITTEE MEMBER ROBERTS: Yeah. Obviously, it didn't apply to me this time around, but I really like the idea of having the actual original papers provided in electronic form, because I like to go back to those. And the fact that they're in electronic form saves a lot of paper and lugging around to the meetings.

From what I understand, it's not that the one really good paper publication report or study wouldn't necessarily rise to the above. It's where you may have

very few studies or very small groups sizes, very poor characterization of -- you know, the sorts of things that we have discussed up here that would sort of drop down maybe confidence level it.

I guess what I'd say is that the organizations that might be more pro-listing would -- if you minimize -- if you put something together that does not go into the same comprehensive depth as the other portions, say if it was female repro and the developmental and the male are very comprehensive, and say, as an example, the female was not, that organizations that might be concerned that that would be overlooked would need to have an opportunity to put together a more comprehensive set of comments.

But I would think, since you come out with these months in advance of our meeting, that that would provide that opportunity, wouldn't it?

DR. DONALD: Yes. One thing we would encourage the Committee members to do is once you've seen the materials and had a chance to look at them, please feel free to contact us individually. I know we can't have serial meetings, but individual members are welcome to contact us. In fact, we encourage you to contact us with any questions you have, particularly in advance of the meeting, because sometimes, you know, if a complex question comes up at the meeting, it's difficult for us to

give you a complete answer. But if we have some notice, we can research the question and provide whatever information you need, either in advance of the meeting or at the meeting.

Dr. Kaufman was one of the principal authors of the sulfur dioxide document, and actually came up with several of the ideas that were incorporated into the document. So she can describe how we've already -- or how we thought we'd already taken some steps in the direction we're talking about today to try and sort of -- not exactly create the hierarchy of the material, but trying, and help identify what we thought was the most useful information for you.

DR. KAUFMAN: So we would really appreciate feedback on that, as Dr. Donald said, about the format of the HIMs. And sulfur dioxide was such a huge body of literature, that when we approached it, we tried to reformat it, so that as he mentioned earlier, it kind of was a hierarchy where there were tables that were incorporated in this HIM to give you an overview, almost a roadmap of the studies in that endpoint.

And along with it, there were summaries of that endpoint early on. And those were related to the actual more extensive study summaries that we included in the appendices, and as well we gave you the articles on CD.

Thank for, Linda, for noting that was very useful to you. It's good feedback for us.

So when we wrote them up, all the study summaries, the study designs varied extensively, and there were, you know, much better design cohort studies and more reliable. And there were also ecologic studies. So we focused more of the -- more extensive summaries of the study designs that are -- instill more confidence.

The ecologic studies, for instance, we didn't write extensive summaries. And in some cases, we just mentioned briefly in a paragraph what they were about, and just left it at that, because they are not that informative.

So that's how we tried to incorporate the information in a very -- in a more digestible manner and tiered. So if there's any comments you have about one part or the other or if there's a better way to do it, if -- anything that you can give us guidance on would be appreciated.

COMMITTEE MEMBER KLONOFF-COHEN: I appreciated the table, because I usually make tables. That would have just taken hours and hours for this topic, so that was really helpful. But overall, just all of the different hierarchy of how you set it up, I just thought it was really great.

COMMITTEE MEMBER WHITE-PORTER: I'd agree. I thought the format was wonderful. I'm reading documents from physicians all day long. I'm reading, reading, reading all day, and the format really was easier for me to organize, very easy to work through. I liked the -- I loved the appendices. I highlighted. I knew where to find information on the abstract if I needed to read the document further. I loved it. It was great for me.

Thank you.

CHAIRPERSON BURK: I agree. I loved those tables. You know, I think bottom line, your judgment on how to approach it is fine, as long as the actual articles are all mentioned and all given to us electronically. I realize you don't want to make great judgment calls, but you know, if there's something that doesn't have much information, it's not worth writing up a whole page summary of it. So I would support you using your judgment on that, and us too.

COMMITTEE MEMBER KEEN: Just a quick request. I don't know if you could do this due to copyright issues or not, but if along with that CD, there is actually a hyperlink so there was on-line access, I would be one very happy person, because many of us travel around a lot today. We no longer carry disc drives with us. I certainly don't. And so if you just happen to be at, you

know, some red carpet club, and you decide to do some homework, that's the way it's being done, just like going to PubMed. So as long as you can do it, I think you'd find it used by a lot more people.

DR. DONALD: Yeah. We will certainly include those as far as we can in future documents.

COMMITTEE MEMBER KEEN: Thank you.

DR. ZEISE: Another way around that issue is to provide thumb drives. So that might be another possibility, so I just throw that out as a possibility.

COMMITTEE MEMBER KEEN: I think that is an excellent idea. My only comment would be there's a little more fluidity if you're putting them directly on-line access, because you could have materials that then you can be updating, in theory.

ACTING DIRECTOR ALEXEEFF: I'm not sure what's possible with our IT folks. But I know that, for example, just like when you're reviewing a publication for a journal, there's a confidential site you can go to. So with that -- was that the kind of thing you're also talking about if -- I don't know if we would be able to create a specific site that you would have access to for those materials, if there is a copyright issue.

COMMITTEE MEMBER KEEN: That's precisely what I was thinking. Something like the PubMed is a good

example, where if you're on your home campus where they have journal subscriptions, you can directly access it, but if you're at home, you can't directly access it.

So it does need -- and that's why I was careful to say, if you can do this, because there would have to be some agreements probably with documents download, I think, but it would -- I just think it would be very helpful, and it would make it easier for a lot of people and would save paper.

DR. DONALD: Yeah. So one possibility might be if we could create a password protected page on our website where we posted all the PDFs from a document and provided the password to the Committee. We can look into options like that.

DR. ZEISE: Yeah. Just getting back to one other question around the appendices. So it seems as if they were very useful. Now, for some of the studies, they don't carry much -- the studies that don't carry much weight, it might be a staff savings to actually put in the author's abstract and note it as such. Is that something that would be agreeable to the Committee, in cases where it didn't appear necessary to go through and discuss at length the particular studies, just because of quality issues and so forth?

CHAIRPERSON BURK: I think it is, as long as you

have the actual document.

DR. ZEISE: Right. You would have the article itself.

CHAIRPERSON BURK: Then we can make our own judgment as to whether we want to read it or not.

DR. ZEISE: Yes.

CHAIRPERSON BURK: And that would save you a lot of time, just take the abstract out which, you know -- and then we can make that decision.

DR. ZEISE: Great. Thanks.

CHAIRPERSON BURK: I don't know. That seems fine to me. The information is there, but you're not spending lot of time trying to digest it for us, when it's not necessary.

Public comment on this?

DR. LAWYER: So this way you get two-thirds of the public to comment in one day. It's Dr. Artie Lawyer from Technology Sciences Group in Davis, California.

A comment and a question, while we're on this subject. I couldn't help thinking of this matter in the audience. First, the comment on sulfur dioxide, I totally agree with the Committee. That was a great report and it's an amazing thing that these -- that the staff put out, given their resources and such. And I, in fact, was struck, and I told them yesterday, about the quality of

the presentations that was given to the Committee. I thought that was just wonderful.

But it was an interesting session, because there was no public comments on the other side of the issue. And that's what I found myself thinking about in this debate. It's really a question to the Committee. Though -- I'm sure I've been associated with a couple dozen of those, the industry documents that you get before a meeting in the last 30 days, to try to add to what OEHHA has done. I know Jay Murray behind me is I'm sure the winner in being involved in most of these.

But I know we always struggle with trying to get you the right balance between not giving you too much, not being redundant with the quality that you've already received. And I'm just wondering if you have advice for those of us in the public to try to give you an appropriate balance in the documents we give you.

Because I tell you, we always struggle with it. The only thing I'll add is all our clients are different, just like the chemicals we consider. And so sometimes they go along with our suggestions and sometimes not.

But nonetheless, if while you're thinking about the quality that you're asking of OEHHA staff, I'm wondering if you have any advice for, at least the three of us that have remained for the second day.

Thank you.

COMMITTEE MEMBER KEEN: I have to say, I was quite surprised at the minimal public comment yesterday, particularly given the fact that one of the documents was quite exhaustive and really quite thorough, and I thought very well done.

I personally find them a useful counterbalance to the documents that we get from OEHHA. I think it's important to have, if people feel strongly, gee I think this case is way -- is ignoring these points. Then I think that that is a role that the public actually should be playing.

So I, for one, would say, if anything, it wouldn't bother me one iota to see twice as much material there, as long as it's documented and it's not about passion, but it's about science. And you can literally take the public comments and put them in those two piles sometimes. So I would applaud continued authoritative comments from the public personally.

COMMITTEE MEMBER ROBERTS: Yeah. I'd sort of echo that, any comments that we get that are based upon scientific interpretation and give references that can go back and people can look at. That's all very helpful. What doesn't tend to be really helpful to me is if I have page after page of a business impact. A little bit of

business impact is good to understand, but I don't have any expertise there.

CHAIRPERSON BURK: Okay. Any other comments?

I'm going to go to the last agenda item, number 8, Summary of Committee Actions.

George.

ACTING DIRECTOR ALEXEEFF: George Alexeeff here.

Okay. Well, I think the Committee considered and undertook a number of actions these past two days. And I think it was appropriate to have a two-day meeting. So I appreciate you being here both days.

So, first, the Committee considered whether sulfur dioxide should be designated as a chemical known to the State to cause reproductive toxicity. And the Committee did decide to consider it a chemical known to the State to toxicity -- known to the State to cause reproductive toxicity.

Specifically, there was a vote of five yes and zero no with regards to listing it as a chemical known to cause reproductive toxicity with specific reference to developmental toxicity.

The Committee concluded that sulfur dioxide was clearly shown through scientific valid testing, according to generally accepted principles to cause developmental toxicity.

With regards to female toxicity, the Committee concluded as a vote of zero to five that it was not clearly shown. And with regards to male reproductive toxicity, the Committee voted three yes and two no, with regards to whether it was scientifically valid -- was clearly shown through scientifically valid testing through generally accepted principles to cause male reproductive toxicity. And based upon that vote, that endpoint will not be designated as part of the listing.

Regarding the consideration of the petition filed on August 5th, 2010 on behalf of the Polycarbonate BPA Global Group of the American Chemistry Council to reconsider the designation of NTP CERHR as an authoritative body for the purposes of identifying reproductive toxicants, first, the Committee voted six to zero to hear the petition.

After hearing the petition, a presentation from the National Toxicology Program, public comments, and Committee discussion, the Committee voted not to consider de-designating NTP CERHR as an authoritative body. And the vote was zero yes and five no with one recusal to de-designate NTP CERHR.

The Committee then voted to wait to consider designating the NTP Office of Health Assessment and Translation as an authoritative body. And the vote on

that motion was six yes and zero no to wait on revising the NTP designation.

Regarding prioritization of chemicals for future Developmental and Reproductive Toxicant Identification Committee review, the Committee recommended that OEHHA proceed with the five chemicals proposed benzo(a)pyrene, deltamethrin, methyl parathion, uranium, and xylene, and providing us some sense that benzo(a)pyrene appeared to be the most important one to prioritize with the others with less importance.

And finally, the Committee also considered removing nine chemicals from the list of chemicals that have not been adequately tested as required. And the vote was six to zero in favor of removing the nine chemicals from the list. And I'll just read them for the record, 4-T-amylphenol, aquashade, benzisothiazolin-3-one, ethoxyquin, irgasan, magnesium phosphide, niclosamide, spinetoram, and sulfometuron-methyl.

So I think that those were the official actions taken by the Committee, unless I've missed something.

All right. I want to again thank the Committee for taking valuable time out of their schedule to serve the State and provide the State advice and to assist us in this reproductive toxicity issue or all the issues under this topic. And I thank Dr. Burk for chairing the

Committee and dealing with a lot of, you know, different types of issues this time and being able to move us along and keep us focused, and being responsive to the public concerns before about timeliness of comments and things like that.

And I also want to thank all the Committee members for their assistance in considering -- excuse me, in considering the documents -- and I felt like I was always looking over here, so I figure I should look over here.

(Laughter.)

ACTING DIRECTOR ALEXEEFF: I was not ignoring this side -- in considering documents and providing thoughtful comments. And I really thought the discussion on sulfur dioxide as well as the other chemicals were very interesting, thorough, productive, and thoughtful. And I appreciate all of that. And I think it shows a good record of decision for this meeting.

So I want to thank you again.

Oh, did I forget to thank the staff?

(Laughter.)

ACTING DIRECTOR ALEXEEFF: Yeah. The ones once I have to go see after this meeting.

(Laughter.)

ACTING DIRECTOR ALEXEEFF: I do want to thank the

Counsel, Carol, for giving us advice during the meeting. She had quite a few presentations to make and clarifications and answer questions. I really want to thank that.

And I want to thank all of the staff for the presentations, Dr. Zeise and Dr. Donald, Dr. Kaufman, plus the entourage, some of which are behind there, that helped assisting and preparing the documents and the presentations yesterday. And I'm glad that you thought the documents were well done and the presentations were well done. And I definitely thought so as well. So I also want to thank the members of the public that participated with us yesterday and today, and on the webcast I presume there's some as well.

Thank you.

CHAIRPERSON BURK: All right. I echo all those thank yous. And the meeting is adjourned. Safe trip home.

(Thereupon the Developmental and Reproductive Toxicant Identification Committee adjourned at 10:19 a.m.)

CERTIFICATE OF REPORTER

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

That I am a disinterested person herein; that the foregoing California Office of Environmental Health Hazard Assessment, Developmental and Reproductive Toxicant Identification Committee was reported in shorthand by me, James F. Peters, a Certified Shorthand Reporter of the State of California, and thereafter transcribed under my direction, by computer-assisted transcription.

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

IN WITNESS WHEREOF, I have hereunto set my hand this 18th day of July, 2011.

JAMES F. PETERS, CSR, RPR
Certified Shorthand Reporter
License No. 10063