MEETING

STATE OF CALIFORNIA

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

PROPOSITION 65

CARCINOGEN IDENTIFICATION COMMITTEE

JOE SERNA JR.

CAL/EPA HEADQUARTERS BUILDING

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SIERRA HEARING ROOM

SACRAMENTO, CALIFORNIA

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10:00 A.M.

JAMES F. PETERS, CSR, RPR
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APPEARANCES

COMMITTEE MEMBERS

Dr. Thomas M. Mack, Chairperson

Dr. David A. Eastmond

Dr. Solomon Hamburg

Dr. Martin L. Hopp

Dr. Joseph Landolph

Dr. Anna H. Wu

STAFF

Dr. Joan E. Denton, Director

Mr. Allan Hirsch, Chief Deputy Director

Dr. George Alexeeff, Deputy Director

Ms. Carol Monahan-Cummings, Chief Counsel

Dr. Jay Beaumont, Cancer Toxicology & Epidemiology Section

Dr. Jennifer Hsieh, Cancer Toxicology & Epidemiology Section

Dr. Martha Sandy, Chief, Cancer Toxicology & Epidemiology Section

Dr. Rajpal Tomar, Cancer Toxicology & Epidemiology Section

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

APPEARANCES CONTINUED

ALSO PRESENT

Ms. Jeanette Bajorek, FAN

Dr. Robert Barter, ExxonMobil Biomedical Sciences

Mr. David Boothe, FAN

Dr. Derek Gammon, FMC Corporation

Mr. Danny Gottlieb, Citizens for Safe Water in Modesto, California

Mr. Jeff Green, Citizens for Safe Drinking Water

Mr. J. William Hirzy, National Treasure Employees Union, Chapter 280

Dr. Sarah Janssen, Natural Resources Defense Council

Dr. David Kennedy, International Academy of Oral Medicine and Toxicology

Dr. Gerald Kennedy, DuPont

Mr. Stan Landfair, DuPont

Dr. Jay Murray, Consumer Healthcare Products Association

Dr. Lisa Navarro, Ciba Corporation

Mr. Chris Neurath, American Environmental Health Studies Project

Dr. Howard Pollick, University of California, San Francisco

Ms. Renée Sharp, Environmental Working Group

Dr. Annette M. Shipp, ENVIRON International

Dr. Fernando Suarez, Syngenta Corporation

Dr. Gary Van Riper, International Molybdenum Association

INDEX

PROCEEDINGS

DIRECTOR DENTON: Since we have all of our committee members present, I just have a few opening remarks and then I'm going to turn it over to our Chairman, Dr. Tom Mack, to conduct the meeting.

First of all, let me introduce the panel members. To my left is our Chair, Dr. Tom Mack; and to his left is Dr. Anna Wu; and then Dr. Joe Landolph is at the far end.

To my right, is Dr. David Eastmond followed by Dr. Marty Hopp; and then at the end to my far right is Dr. Solomon Hamburg.

Dr. Darryl Hunter, who is also a member of this committee, was unable to attend today. So this is the panel members, which will be participating in the meeting today.

All of you know, but I'd like to repeat, that this is the second time that OEHHA has had the opportunity to solicit the advice of the Carcinogen Identification Committee on prioritization of chemicals for development of hazard identification materials. And this process basically follows our 2004 prioritization document.

We have 38 chemicals, which we are soliciting advice and recommendations from the Committee on today, and those committees -- I'm sorry, and those chemicals passed either the human screen or the animal screen. And

again, the procedure is very well outlined in our prioritization document. And I'm assuming that everyone here in the audience is familiar with that.

So I want to make a comment about the agenda. The Committee will be considering batches of chemicals. As they go through the 38 chemicals, there will be Committee discussion, in which there will be an initial relative ranking of chemicals of all the 38 chemicals. And, at that point, we're going to take a break.

The main purpose of the break will be to give you and the audience an opportunity to, having heard the discussion, decide whether or not you want to provide oral comments or if you've already decided and turned in a card to Cindy. Cindy is the keeper of the blue cards, which indicate individuals who want to provide public testimony.

If you decide, at that time, you've already turned in a card and you decided that you don't want to make comments, then you can withdraw your comment card at this time.

But these comment cards help us kind of keep organized and sort of run through the meeting smoothly. So at any rate between the Committee discussion and the actual official public comments at the mike here, there will be a 10 minute break.

So with that, I would like to turn it over to our

esteemed Chair, Dr. Tom Mack.

CHAIRPERSON MACK: Thank you, Joan. Are you hearing me?

In contrast to my usual free-wheeling style, I'm trying to impose some discipline on myself this morning. And one of the features of that discipline is to read you a little preamble, a little position paper about our first task today, which is a difficult one.

The prioritization of chemicals is based on a number of imponderables. And one of them is the magnitude of the exposure to the people of California, both past and present. And the table that you have in front of you that OEHHA people have provided is a very inadequate summary of that, but it's the best that they or we could do.

Not only should the decision involve the prevalence and intensity of exposure, but we have to keep in mind whether or not there are particularly vulnerable populations, like kids or pregnant women, and/or populations, which, to some extent, are voluntarily or in some other way assigned the exposure, which is occupational exposures.

A second issue is whether or not there is enough available scientific information to make a reasonable judgment about whether or not a compound is, in fact, a carcinogen, whether it be of animals or people. And again

the survey -- the table that you have provides Xs, which says whether or not there is information of a given kind for a given compound.

All of these compounds expose somebody in California. And all of them have some kind of information available, which means it's not a matter of whether or not we actually make a judgment about listing. It's only a matter of when. So this is strictly a prioritization. Not a, if yes or no, it's simply a matter of which comes first.

And there's a third issue besides the exposure issue and the presence of information issue, and that is the presence of authoritative body judgments. You know that if an authoritative body deems a particular compound to be a carcinogen, that's adopted by the listing process without our having to make a separate decision.

Most of the chemicals on this list have been addressed by authoritative bodies at one time or another. And it stands, logically, that they haven't been judged to be carcinogenic by those authoritative bodies at that time.

Now, obviously some of these discussions and some of these times were in the distant past. Some of them were in the relative recent past. So the availability of studies that might contribute to our understanding of

carcinogenesis may well have happened subsequent to that discussion.

And then we come to the bear, the elephant in the room. And the elephant in the room is quality of the individual studies. We cannot discuss the quality of the individual studies today. We cannot discuss it, because if we started to do that, it would take three weeks. There are 38 different compounds. There are six people up here and a lot of people down there and a lot of information is in the minds and the notebooks of all the people up here and down there.

If we start discussing an individual compound, we simply will start to go through the listing process and that's not what we're going to do today. So I would beseech you not to plan on discussing the quality of studies when you come to the public comment section. I want you to tell us if you know of something that we don't know about the presence of a study of a certain kind that isn't -- doesn't have an X in the chart in front of you, or whether you have some opinion or knowledge about the exposure to the people of California. Those are both very pertinent. I think we probably have an accurate description of all of the authoritative body judgments in front of us.

So our discussion will not involve the quality of

the studies. They will only involve the existence of the studies, the exposure distribution as best we know it, and the timing of the authoritative bodies, and the subsequent studies.

So when the public comment section comes up, again, I'd like you to provide information if you've got it available to us to help us with two things, the exposure and concern about exposure to the people of California on the one hand. And on the other hand, whether or not there is some study that we don't know about, the existence of some study we didn't know about.

And I think that completes my little harangue. I will tell you that one of the things I've learned today and that I've learned to be respectful and afraid of more than I had ever in the past is very large 3-ringed binders.

(Laughter.)

CHAIRPERSON MACK: I can't stand them, and we had to deal with a lot of them in this process.

Okay.

DIRECTOR DENTON: Okay. Any preliminary comments from OEHHA staff?

Thank you. I think you're good to go.

CHAIRPERSON MACK: All right. We'll start with the chemicals that have been assigned to me.

And so I'll mention the exposure situation and mention the authoritative body situation and the availability of studies situation and then make a listing. There's a question back there.

You can't hear me?

DIRECTOR DENTON: You have to speak right into it.

CHAIRPERSON MACK: I have to speak right into it like that?

All right. Okay, the first one on my list in the order that they're present on that table is molybdenum trioxide, which has relatively limited exposure in California. And then generally on an occupational basis. There is at least one analytic human study. There is availability of studies which discuss animal data in two or more categories. And there is evidence pertinent to genotoxicity.

So I would deem that study to be relatively limited in terms of exposure, but with available information. And I would categorize that arbitrarily, but as best I can in the middle category. Not high priority, not low priority, but middle priority. Downgraded because of the relatively limited exposure, upgraded because of the availability of studies.

Now, I know that's pretty simple minded, but

that's the best, I think, we're going to be able to do.

The next one that I have on my list is rock wool. Rock wool is again relatively limited in terms of exposure. There is an analytic study, at least one analytic study. There is studies of several animal studies available and there is evidence on the issue of genotoxicity and other short-term tests.

That compound was reviewed relatively recently by IARC. And subsequent to that review, there is very little additional evidence, if any. So I would designate that as being low priority for this committee.

The next one on my list is 11-Aminoundecanoic acid. That is designated as high exposure in some people. There is no animal -- there is no human evidence. There is animal evidence. There is evidence pertinent to short-term tests. And because of the unavailability of human evidence, I've designated it as being middle also.

The next one I have is 2-Chloro-1,1,1-trifluoroethane. Some occupational exposure. Animal evidence is limited. There is evidence on short-term tests. And I designate that as being low exposure. And that's also because that's been reviewed by authoritative body without any additional information available.

Next I come to fluoride and its salts.

Obviously, a very, very important exposure to the people of California. This time there is available human evidence. There is also available animal evidence. This was reviewed by authoritative bodies, but not very recently. And there is at least one important study or one study of humans, which has come up since the availability. So I would designate that as high priority for our body.

The next one on my list is haloperidol, which is a compound that may expose some people undergoing anesthesia, but at very low levels. There's no human evidence. There is some animal evidence. There is evidence on short-term testing. And I would designate that as right on the cusp between high and middle actually. So let's call it high, because it involves people who are getting anesthesia. There is no authoritative body information.

Actually, that does it. That's all six of my compounds. Now, I think what we'll do is after each of us finishes our list of six, we'll ask the other members of the Committee if they have any comments on those six. And any suggestions for changes. And then after that, we'll go to the next person. So let me ask my colleagues on the Committee, if there are any alternative suggestions for the ones that I've listed.

Seeing none, we'll go to the next person. Anna, would you be willing to be next?

COMMITTEE MEMBER WU: The first one on my list is amphetamine and its salts. And it's used in many various types of medications. And in terms of exposure, it is high in frequent users. In terms of analytic studies, there are actually at least 10 studies covering various cancer sites in adults as well as in children.

In terms of animal studies, there is one that looked at tumor initiation and promotion. And then in terms of other relevant data, there are both genotoxic and other mechanistic studies.

And based on the human analytic studies as well as in terms of the exposure, I would classify this as high. The second on my list is -- well, actually I'm doing them alphabetically, sorry.

The second one is D&C Yellow #11. This is a color topical in many drugs and cosmetic preparations. So the exposure is widespread. There are no analytic study -- or no studies in humans. There are at least two or more studies in animals and there are also genotoxic studies. And I would put this in the low to middle category.

The third compound --

DIRECTOR DENTON: Anna, probably it would be best

if it was either in the low or middle, because we haven't --

COMMITTEE MEMBER WU: Then I'll put it in low.

The second on my list is -- I mean, the third on my list is dicofol. I don't even know how to say it. Anyway, this has -- this is widespread. In terms of exposure, it has two recent publications: One a descriptive study in children; and one an analytic study in children. There are animal studies in one site. And there is a number of relevant data, both in terms of mechanistic studies, hormonal activity disruption and other compounds similar to this one.

And I would -- and this was actually reviewed by IARC in 1982 and by U.S. EPA in 1998. But the two studies in humans and in children that were published was in 2005. And I would say that this is in the middle category.

I want to say middle and high, but I know you said not to. But, I mean, that's really how I feel middle and high, but anyway.

The fourth on my list is methoxychlor.

This one is widespread in terms of exposure. There is one analytic study published in 1990 and then a new descriptive study, analytic in human, that was published in 2006. There's animal data in two or more studies. And there are also other relevant data. And

this was reviewed in 1979 by IARC and by U.S. EPA in 2003. And I would put this in the middle category.

The fourth on my list is triamterene. It is in various medications. It is high exposure in those who use it. There are no analytic studies. There are at least two or more studies in animals and the genotoxic data, and I would put this in the low category.

The last on my list is vinylidene chloride. There are limited exposures in those who are exposed at work. There is a study from 1976. And this was reviewed in a summary article in humans. There are at least two or more studies in animals. And there are genotoxic as well as structural similarity studies that are relevant. And this was reviewed in 1986 by IARC and I would put this in the low category.

CHAIRPERSON MACK: All right. Do any of the members of the Committee have any comments to make on those rankings?

All right. Joe, would you like to go next.

COMMITTEE MEMBER LANDOLPH: Sure.

Yeah, the first one on my list is aspartame. And I struggled with this one a little bit. I read a lot of the public comments as well. It's an artificial sweetener found in over 6,000 products, used by over 200 million people worldwide. So certainly in California it's used a

lot too.

Presence of the studies shows a lot of human use. There are three epidemiological studies, time-related studies, cohort studies, case control studies.

DIRECTOR DENTON: Joe, they can't hear.

COMMITTEE MEMBER LANDOLPH: They can't hear? Okay, I'll be louder. Sorry.

And there are a number of animal studies, long-term diet studies in rats. There are three of them. And evidences of tumors coming up in there. Transitional cell carcinomas of the renal pelvis.

Authoritative body studies, I couldn't find any.

Genotox studies, the usual mutagenesis and unscheduled DNA repair synthesis are negative. There are positives for chromosomal aberrations and sister chromatid exchange. And it's metabolized to aspartic acid and methanol and phenylalanine.

So I guess I come down on the side of this of unfortunately somewhere between low and medium. So I'm going to come down on medium. It's a difficult one to deal with and the data is not great. But I think maybe we take a small look at it would be appropriate.

The next one was benoxacor. The nature of the exposure, mainly it's an inert ingredient in herbicidal formulations containing metalachlor. And it's used in

greenhouse flowers, corn, soybeans, peanuts, et cetera. So exposures occur occupationally in that setting and by consumers buying treated flowers and eating treated food crops. So there is some significant human exposure there.

No epidemiological studies.

There are two animal studies.

Authoritative bodies. Yes, the EPA did look at benoxacor. And they said it cannot be determined whether it is carcinogenic or not, but it was suggestive, so they're obviously struggling with this too, based on increases in non-glandular forestomach tumors in male and female mice and rats. But these tumors have questionable relevance to humans. So they're sitting right on the fence. And there are also ovarian cysts induced in female mice and rats, but they're not malignant.

The genotoxicity data is pretty much negative for it across the board. So I put this in the low category for study.

The next one was triclosan. Everybody knows about triclosan. It's a synthetic broad-spectrum antibiotic. It's used in many products, hand soaps, everyday products, deodorants, toothpaste, laundry detergents, facial tissues, diapers, kitchen utensils, et cetera. So it's all over the place. A lot of human usage.

Presence of study. No epidemiology studies. Rat study was negative. Hamster was negative. Mouse study was positive in males and females in the liver, which always leads to arguments as to whether that has human relevance.

The authoritative body studies. The EPA ruled it as not likely to be carcinogenic to humans. And their rationale was that it stimulates the PPAR-alpha receptor and gives liver cancer in mice. And their argument was that quantitatively it would be implausible that it was carcinogenic to humans. Those arguments are not incredibly strong. They are logical, but they're not incredibly strong.

So overall, I rank that in the low category for triclosan.

The next one was tris(1,3-dichloro-2-propyl) phosphate. And the nature of exposure. It's a flame retardant. And it's used in foams, resins throughout the U.S. and Europe. It's incorporated into polyurethane foam. And it replaces pentaBDE. And it's used to treat fabrics and upholsteries. So the general population is exposed by inhalation, dermal exposure. Where these materials were treated with this are found, in homes, offices, wherever people contact tris-treated upholstery, there can be potential exposure. Automobile and truck

upholsteries and draperies, et cetera.

Presence of the studies. No cancer epidemiology.

Animal studies. This one had stronger animal studies. There was a rat study, where they had renal tumors in males and females. Male testicular tumors, which was dose-dependent. Hepatocellular tumors in male and females and cortical adenomas. So this had a strong animal database.

Genetox was pretty much negative.

Authoritative bodies not evaluated by IARC nor EPA.

Most of the genetox data is negative.

So I ranked this one in the medium category, based on the strong animal studies and multiple tissues in dual species.

The next one was tetrachlorvinphos. Nature of exposure. On organophosphate insecticides, used on pet flea and tick collars. Used in agriculture. Dermal application to livestock, larvicide in cattle, et cetera. Used on crops, cotton, grains, fruits, vegetables.

Occupational exposure occurs where it's used or applied on farms, ranches, poultry houses. The general population may get exposed to it, when they apply pet collars or powder to their pets or for certain residential usage. So there is usage and exposure to the general

population.

Presence of the study. No cancer epidemiology. There were animal studies. Let's see two in mice. And long-term dietary studies in rats, two of those. And there were tumors of the thyroid gland in the rats.

Authoritative bodies. In 1983, IARC indicated that there was limited evidence for the carcinogenicity in animals. And insufficient evidence for carcinogenicity in humans.

And the female and male mice studies showed a dose-dependent hepatocellular carcinoma induction. There was some genotoxicity in yeast and mouse bone marrow, so there was some genetox data.

And I think that's it. So overall I listed it as medium for consideration. And I think that -- I still have two more.

The next one N,N-diethylthiourea.

Nature of exposure. It's a corrosion inhibitor in ferrous metals and aluminum alloys, used in vulcanization acceleration in rubber manufacture, and in some types of paints. You see exposure in the occupational setting. And to consumers that are in contact -- that contact products containing this material, particularly people using rubber wetsuits, because it's contained in the rubber. So there is some human exposure.

Presence of studies. No epidemiology studies were found. Animals negative. NCI mouse study. Feeding study in rats where they get follicular cell carcinomas and thyroid tumors in the males. And follicular carcinomas in males and females.

Authoritative body listing. IARC listed it is as Category number 3, which means it can't be determined whether it's carcinogenic to humans. Limited animal evidence for the carcinogenicity. Inadequate evidence in humans for the carcinogenicity.

And I have more extensive notes, but based on that and the genetox data added together, I listed it as low for consideration.

The last one I have is permethrin. Nature of exposure. It's a Type I pyrethroid insecticide. General use pesticide used on food and feed crops, tree nuts and lettuce, on livestock, pets, clothing, structural pest control residual use, mosquito abatement, and to treat head lice and scabies. So there is exposure to the general public and workers in the occupational setting that are also exposed.

Presence of the studies. Again, no cancer epidemiology. Animal studies, there actually are a number of studies done. There's one, two, three, four, five mouse studies and two rat studies. And there are some

positive in the mouse studies for benign and malignant tumors. The rat studies seem to be pretty much negative.

The EPA has dealt with this. And they said it's likely to be carcinogenic by the oral route in 2002. In 1990, WHO said the oncogenic potential was low. Occurred in the male mice. Probably an epigenetic acting agent. In 1991, IARC said it was inadequate for carcinogenicity data in animals and not classifiable for humans. And then the last one, EPA said it was likely to be carcinogenic to humans by the oral route.

Let's see, the genetox data is pretty much negative. There's ambiguous data for clastogenesis. And no epidemiology data on this at all.

So I rank this one in the medium category, based on a number of positive animal studies.

That's it.

CHAIRPERSON MACK: Okay. Does anybody on the Committee wish to comment on those rankings?

All right. David, would you go ahead now.

COMMITTEE MEMBER EASTMOND: Okay. Let me start with diethanolamine. And just give everyone a second to get there. Diethanolamine has widespread usage, primarily as component of metal working fluids. So it's estimated that over a million people in the U.S. are exposed. So exposure is quite -- certainly high, and it's an

occupational exposure. But also I believe it's found in consumer products as well.

NIOSH concluded there was substantial evidence linking these metal-working fluids with various types of cancers. But there are many other components of these metal-working fluids, so it can't be attributed directly to diethanolamine.

In animal bioassays, it's tested by the National Toxicology Program in mice and rats. It was positive in -- with certain types of -- several types of tumors within the liver of the mice. And also kidney tumors were seen in male mice.

No tumors were seen in the F344 rats. And there was no increase in skin tumors seen in a transgenic mouse model for cancer.

So there's actually been some work on mechanisms. And it's believed that mode of action is -- at least there's a plausible mechanism for the mode of action for the liver tumors, which is believed to be much -- and for this mode of action, the animals are -- the mice are believed to be much more sensitive than the rats. And both of those would be more sensitive than the humans.

Anyway, this has been reviewed previously by IARC. And they placed it in Group 3 as not classifiable. They consider the animal evidence limited and human

evidence inadequate.

The NTP did indicate that there was clear evidence of carcinogenicity in the male mice and the female mice, but not in the rats. But the NTP has not listed it in the annual review of carcinogens.

Looking at this, I put this in sort of the medium category.

The next one is diisononyl phthalate.

This is a plasticizer used in various consumer products. And of most concern infants and toddlers are most exposed, due to its use in soft toys and other similar products. There's a lot of hand-to-mouth sorts of things. So concern about widespread exposure and particularly in children.

There were no real epidemiological studies available.

But there were some animal studies. In one study conducted by Covance, using rats, there were liver cancers, and mononuclear cell leukemias, which were seen in both the female and male Fischer 344 rats.

Renal tubular carcinomas were also seen in the male rats. There was a follow-up -- or another study. It was done by Lington. And they saw liver cancers seen in the high dose in Fischer 344 rats. They also saw mononuclear cell leukemia in both male and female rats.

And in mice hepatocellular carcinomas have been seen in male and female mice. So there's quite a bit of evidence in animal models for different types of tumors.

The phthalates are proposed to act to cause their liver tumors through a mechanism involving PPAR-alpha, peroxisome proliferation receptor alpha. So these act as agonists on the receptor and stimulate proliferation. There is some question right now about whether that mechanism actually is true. Some of the phthalates have been tested in PPAR knockout mice. And they still cause liver cancer. So there's -- what was thought to be a well established mechanism, may not be really correct. This has not been reviewed by IARC. And the EPA had expressed some concerns about carcinogenicity.

Because of the animal studies and the positive results seen and particularly the widespread exposure and particularly the exposure to children, I would put this in the high-priority category.

The next one is hydroquinone. And I should mention that I have done some studies on hydroquinone on the genotoxicity of hydroquinone, just for the record, but I don't think it would influence things too much.

Hydroquinone is widely used as an industrial chemical. It's actually used as a pharmaceutical for skin lightening in certain cases. It's a natural product or

can be formed from natural products in your stomach during acid hydrolysis. And it's also a metabolite of the well known carcinogen benzene.

There are a number of epidemiological studies that have been conducted, but none of those detected significant increases in cancers.

The National Toxicology Program tested hydroquinone in their animal bioassays. And it was reported to induce hepatocellular adenomas in the male mice in one study and in female mice in another. So that's two different studies. And in rats, it was induced renal cell adenomas in two studies.

So the NTP concluded that there was some evidence for tumorgenicity in the male rats due to renal adenomas and some evidence in female rats due to mononuclear cell leukemia, and some evidence in female mice due to hepatocellular tumors.

Another study by Shibata et al. reported that hydroquinone-induced hepatocellular adenomas in male mice and renal adenomas, which they thought were really due secondary to nephropathy toxicity in the kidney in the male rats. So there are some reports. Now these tend to be at very quite high doses with hydroquinone where you see these effects.

IARC has evaluated hydroquinone and concluded

that there was inadequate evidence in humans and limited evidence in animals. It was placed in Group 3, which means it's not classifiable for carcinogenicity in humans. It has been implicated -- hydroquinone has been implicated in some mechanistic studies of benzene. But clearly, the benzene story involves other issues. Hydroquinone alone is not responsible for benzene, but it may play a role in combination with other metabolites.

And there is some limited evidence of carcinogenicity of 1,4-benzoquinone, which is a metabolite of hydroquinone. Some fairly obscure studies. But just because I work in this area, I'm familiar with it.

Given the animal tumor evidence -- oh, I should say it's been tested in a wide range of genotoxicity studies. It tends to be clastogenic in vitro and in vivo when given by IP administration. That's because there's efficient detoxification of phenolics in the intestine and liver. So the benzene -- people who work with benzene try to bypass those, because you're looking at metabolism formed in the liver. But from a human exposure point of view, there's certainly an added level of protection because of Phase II conjugation in the liver and in the intestine.

Anyway, I put this at sort of medium priority.

The next one perfluorooctanoic acid PFOA, and

related products.

This compound has widespread exposure due to its use in water repellant, teflon, other industrial products. So there's widespread exposure. It's actually quite -- there's concerns because of some accumulation in biomonitoring studies that have been seen, the presence of PFOA in individuals. So there's certainly concern among the public about this compound.

With regards to the epidemiological evidence, there have been a number of studies. They don't seem to show really very consistent results. One study showed an increase in prostate cancer associated with exposure. But a follow-up study, which has more accurate exposure estimates, did not -- was not able to confirm that association. It essentially disappeared when they used more accurate exposure estimates.

And there was a report of a non-significant increase in liver and bladder cancer, in a PFOS manufacturing facility. But again a follow-up study provided little evidence for the bladder cancer risk. So there's some suggestive stuff in the humans, but not really consistent or no consistency that I can see.

In a dietary study in rats, there's some evidence that PFOA is carcinogenic, inducing liver adenomas. I guess there's -- modest increases were seen in two

studies. Leydig-cell tumors were seen -- increase we're seen in two studies, and pancreatic tumors. These tend to be adenomas I believe.

These were actually seen in one study, the second study. And then they went back to the first study and there was some supportive evidence for that. It's kind of a judgment call on whether you fall on one side of the line or the other. There was also an increase in mammary fibroadenomas that did not exceed historical controls, so that was not considered to be super strong.

This compound is generally negative in genotoxicity tests. Although, it has been reported in a number of studies to cause chromosomal aberrations in polyploidy in vitro.

According to the EPA Science Advisory Board, there's evidence that PFOA hepatic effects are due to this PPAR agonism, and that the Leydig-cell tumors and the pancreatic tumors probably did not represent a significant cancer risk due to differences with receptors and toxicodynamics between rats and humans.

There have been some other studies. PFOA has been tested actually in a trout model. And there was reported acts as a tumor promoter. And mechanistically, they believed it didn't act through PPAR-alpha peroxisome proliferation, but it was working through an estrogenic

signaling. I believe this used some microarray approaches to doing this.

So I'm not sure about the latest. I believe the EPA Science Advisory Board Panel in 2005, this was a draft report, thought that it likely was carcinogenic in humans, but I don't know if that's been finalized or how that's played out.

Anyway, I look at this -- for me, this is driven -- I think the human epi is pretty inconsistent. The animal studies are -- there is some reproducibility, not super strong, but they're there. Because of the broad widespread public concern about this, I think it's something we probably ought to put as a higher ranking. So I'd put this in this medium-to-high ranking, which you love.

(Laughter.)

COMMITTEE MEMBER EASTMOND: So I guess in the -- as far as simply because of public concern, I'd probably bump it up into the high, but that's a judgment call.

The next one is thiamethoxam.

I hope I'm pronouncing this right. This is a commonly used neonicotinoid pesticide. It's one of the new classes of pesticides. And in my review, there was no epidemiological studies available. It had been tested in mice and rats. It was negative in the rats. However, the

EPA Science Advisory Board concluded that the rats had not been tested at a sufficiently high dose.

And so that an MTD had not been achieved, so that rats become somewhat debatable. In both the male and the female mice, it was associated with an increase in liver adenomas and carcinomas. So liver cancers.

As far as genotoxicity studies, it's been negative pretty consistently. The mode of action is not clear, but appears to operate through two of its metabolites. And these are basically formed at much lower levels in rats than in mice, and humans, based on liver fractions would be expected to be produced at even lower concentrations than in the rats.

So initially, I think in 2000, the EPA thought that -- classified it as likely to be carcinogenic in humans. However, apparently, there was a follow-up review. There was a lot of additional mode-of-action studies have been conducted. And apparently, after re-review, the EPA decided to list it as not likely to be carcinogenic in humans, because of this difference in metabolism and toxicokinetics.

I looked at this, given kind of the evidence, and put it in the moderate category, simply because of the widespread exposure, and you had things in both male and female mice.

That's the end of mine?

No, triethanolamine.

Triethanolamine, again is -- has extensive exposure. It's used as an intermediate in the manufacture of soaps. And it's one of these used in metal working fluids. So when I mentioned before about NIOSH has concluded there's quite a bit of evidence linking a variety of cancers with metal working fluids. But there's so many things in these metal working fluids that you can't really attribute it to triethanolamine.

But anyway, this compound was tested by the NTP in dermal studies. They reported an equivocal increase in kidney adenomas. They were increased in hepatic tumors in mice. But these could not be interpreted due to infection with helicobacter hepaticus.

There was a follow-up NTP study done in 2004, and they concluded there was equivocal evidence of liver hemangiosarcomas in male mice and some evidence of liver tumors in female mice. There was a follow-up study by another group, which dosed animals in drinking water, and reported modest increases in liver tumors and renal cell adenomas, and endometrial stromal sarcomas. However, these authors did not believe that these tumors were biologically significant.

Triethanolamine was non-mutagenic in NTP genotox

tests. And it's been proposed that they work through a mode of action similar to the diethanolamine. However, it appears to be much less potent than the diethanolamine.

IARC reviewed this and considered there was inadequate evidence. They placed it in Group 3.

And anyway, so in my evaluation, I considered this to be a fairly low priority.

CHAIRPERSON MACK: Thank you, David.

Does anybody want to comment on those rankings?

Okay, Marty, would you like to go ahead.

COMMITTEE MEMBER HOPP: I'd like to go alphabetically, if you don't mind.

Is that better?

I'd like to go alphabetically.

The first one is 2-amino-5-nitrothiazole.

This is a veterinary antiprotozoal agent, commonly used in farms and for farm animals. It's exposure to humans is indirect and has no direct exposure via foods, but there is some exposure to humans via its use in azo dyes.

Better?

Sorry.

So its exposure to humans is, I would call, minimal. There have been no epidemiologic studies associating this with human cancers. This chemical was

reviewed by IARC in 1987 and thought to be of low risk for carcinogenicity.

Since that time, there have been one significant study on mouse lymphoma assays. This has been shown to cause granulocytic leukemia. And lymphomas in Fischer rats, male Fischer rats, and not in female Fischer rats. That is the only significant study since the IARC clearance. Because of the low exposure to humans and lack of any further data since the last IARC review, I put this in a low category for review.

The next that I have is methyl ethyl ketoxime, MEKO, M-E-K-O.

This is an industrial antioxidant. It's an anti-skinning agent in paints. It's also used in multiple adhesives and in boiler cleaners, industrial boiler cleaners.

This is -- again, there is no epidemiologic data to correlate with humans yet on this material. However, chronic inhalation studies in rats have shown primarily methemoglobinemia, which has been associated with lymphomas and leukemias in humans. The direct tumor effect on mice have been on liver carcinomas, over a long period of exposure, particularly about two years of exposure.

And with that increased exposure, I would

consider the incidence of tumors to be moderate, rather than severe after a high dosage.

This has not been reviewed in the past by IARC or any other agency. And I think its carcinogenicity testing is low, and its human exposure is medium. Because of the human exposure, I do think that this would fall in the medium category of evaluation.

Next is nitrofurantoin. This is a very, very common medication used for treatment of urinary tract infections. It's a widespread exposure. I would -- even though it's rated here as medium, I would consider it to be much wider spread than marked here in our exposure categories. It's a fairly common medication, I would say.

This has been a -- it's a primary reason why I believe it's on this list is its relationship with other carcinogens, particularly 5-nitrofurantoin. And it's similarity to that medication -- to that drug itself is very carcinogenic.

However, the nitrofurantoin itself during testing has not been found to be significantly carcinogenic, except for occasional osteosarcomas in a low dose in male rats. This has -- this is one of the more extensively studied antibiotics that's in human use and was reviewed in 1990 and found not to be of significant risk to humans.

Since 1990, there have been one significant study

on injection of the material. And, again, the carcinogenicity at this time was found to be low in rats. And so I would still -- even though this has wide exposure in humans, I think the carcinogenicity studies have not significantly changed since the IARC evaluations. And I would put this in a low evaluation.

Next is N-nitrosoanabasine.

This is a component of cigarette smoke, which is a big topic today. It has wide exposure among cigarette smokers, as well as those exposed to secondhand smoke. This is a -- it falls in the nitrosamine category. Very similar to other nitrosamines that have been evaluated and found to be carcinogenic.

This was reviewed in 1987 and found to have a limited carcinogenicity. Since that time, there have been more genotoxic testing that's been positive. However, it does lack further carcinogenicity testing, which is a little confusing to me.

I think on the basis of its structure and prior carcinogenicity data, as well as the exposure, I would put this in the medium category, not because of any further data that's available, but because of its past data and its wide exposure, I believe.

I think this is a high likelihood of being carcinogenic. My own personal opinion, after looking at

this data.

Next is N-nitrosohexamethyleneimine.

This is an explosive -- this is a material that's found in explosives for military jet fighter planes. This has very, very limited exposure, except if you're a jet fighter pilot.

If you are, I think that there's significant studies here to relate this chemical to tumors of the liver, esophageal tumors and nasal turbinates. I was saying I believe that this has limited exposure. However, the exposure that has been seen -- has created tumors of the liver, esophagus and nasal turbinates.

Better?

(Laughter.)

COMMITTEE MEMBER HOPP: So the summary of this is that the carcinogenicity of this material seems to be high during these studies, but the exposure to humans is limited. But to those humans that it is exposed to, I believe it is significant. And therefore, I would put this in a high category.

Last, but not least, is 5-nitro-o-toluidine.

This is a dye used in the textile industry. And it is amongst other pigments -- in pigment synthesis azo dyes and I think a fairly common usage and exposure and a widespread human value.

This has no cancer epidemiology studies in humans unfortunately. However, it has been fairly extensively studied, the last of which was by IARC in 1990. At that time, it was considered a risk for carcinogenicity. However, it did show some hepatocellular carcinomas, which I think is the biggest concern for this material.

Since the last review of IARC, however, the only significant study that I could evaluate was that in 1994, which again related this material to hemoglobin additives and possible erosion of hemoglobin, but it didn't seem to me to affect, what I would expect, the leukemias or lymphomas or any other hemoglobin or red cell type of carcinogens.

So in view of the lack of further carcinogenicity studies, I would put this in the low category also.

CHAIRPERSON MACK: Thank you, Marty.

Does anybody on the panel want to discuss those priorities?

Okay, then finally, Sol.

Yes, Martha.

COMMITTEE MEMBER HOPP: Did I miss one?

DR. SANDY: Sorry, you missed one. It's the 2,6-dimethyl-n-nitroso-morpholine.

COMMITTEE MEMBER HAMBURG: I'm so impressed that people are watching, I have to tell you.

(Laughter.)

COMMITTEE MEMBER HOPP: Where am I?

Which one did I miss?

I'll pass to him and I'll be right back with you.

CHAIRPERSON MACK: Marty?

COMMITTEE MEMBER HOPP: Yes.

CHAIRPERSON MACK: Perhaps, we could wait till you get that and we'll let Sol go first and then you can put that on --

COMMITTEE MEMBER HOPP: Yes, let Sol go first while I pull this up.

CHAIRPERSON MACK: Right.

COMMITTEE MEMBER HAMBURG: I was going to start by saying there's only 6 of 38 left, but apparently there's 7 of 38 left.

Okay, we're almost done. I don't think I've seen this many organic compounds in one place since organic chemistry.

(Laughter.)

COMMITTEE MEMBER HAMBURG: All right. The first one is Anthanthrene. It's a product of combustion usually from cigarette smoking or from gasoline. It's very widespread. There is no human data to evaluate. Animal data is available. There are a number of studies that have confirmed some low incidence of tumorgenicity.

Genetic data is also available, although relatively poor. The most recent data available is from 1983. And it was reviewed by the IARC in 1983 and 1987.

Because of the lack of significant data, although there was some widespread exposure, I would rank this as low.

The next compound is 1,3-dichloro-2-propanol. That has relatively widespread use. It's found as a solvent for celluloids. It's also present in some foods. Again, there's no human data available. However, the animal data and the genetic data, as well as some of the similarities between other agents make this of some concern. And I actually rank this high.

The next compound is 1,3-dinitropyrene.

This is also a product of combustion. It is a nitrated polycyclical aromatic hydrocarbon. That class of compounds has been noted to have significant carcinogenicity. The human data again is not available. Animal data is relatively weak, I think, and the genotoxicity data, and is available, but also relatively weak. And I would rank this as low.

The next one is ethynodiol diacetate. It's a progesterone commonly found in birth control pills. All the data to date is in conjunction with the use of estrogens. There's very little data available as a single

agent. It does have widespread use obviously. But the data is relatively poor. And I would also rank this as low.

The next agent is 3-monochloropropane-1,2-diol. Interesting agent. It's widespread use is significant. There's a significant amount of data in both animal and genotoxic data, as well as similar data as a carcinogen in other tumor models. That makes it of some concern. And I would rank this as high.

And the last agent I was asked to evaluate is 3-nitrofluoranthene. It is a byproduct of an anesthetic. It has relatively wide use. Human data aren't available. Animal data is fair to poor. There is genotoxicity data as well. And let's see, has it been reviewed in the past?

It was most recently -- there's some new data out from 1999. Since it's relatively common use, I would rank this in the medium level.

And that's my report.

CHAIRPERSON MACK: All right. Are you ready?

COMMITTEE MEMBER HOPP: I'm going to take a break and get it right after the --

CHAIRPERSON MACK: Can't hear you, Marty.

COMMITTEE MEMBER HOPP: This material is not in my current binder. I'll have to get it after the break.

So maybe I can return after the break and give it

to you.

CHAIRPERSON MACK: You guys don't have it down there for him.

DR. SANDY: We do.

CHAIRPERSON MACK: Well, while we're getting it, maybe I can make a remark. Can I do that.

DIRECTOR DENTON: Of course.

CHAIRPERSON MACK: I had hoped to be able to get through the prioritization without discussing the results of studies or the quality of studies. And not all of us were able to do that, which means that I can't, in all fairness, demand of you what I've not been able to enforce upon us.

I would just ask during the comment period that if you disagree with the prioritization, high, medium or low, that you state your disagreement in the comment, if you wish to make it, and provide us with the basis, i.e. the basis of exposure, or the basis of the interpretation of studies. I doubt if there's much difference of opinion about the existence of studies.

But you obviously may change your interpretation based on your interpretation of the study. But since we don't have very much time and since we have 38 items, I would just ask that you be brief and succinct when the time comes, if you wish to dispute the categorization.

Okay. Are you ready?

COMMITTEE MEMBER HOPP: Yes.

CHAIRPERSON MACK: Shoot.

COMMITTEE MEMBER HOPP: The last chemical is 2,6-dimethyl-n-nitroso-morpholine.

This is a nitrosamine that has environmental exposures to -- I'm sorry.

I apologize. This is a cyclic nitrosamine associated with multiple other cyclic nitrosamines. And has widespread industry and environmental exposures in the rubber industry in workshops and metal workshops. Its carcinogenicity is very similar to other cyclic nitrosamines, which means that it's positive in multiple rat studies. Human study epidemiology has been negative so far.

However, on the strength of the animal studies and its relationship to other cyclic nitrosamines, which I particularly don't like, for human exposure I put this in the high category -- high to medium category.

CHAIRPERSON MACK: Okay. Does anybody wish to challenge either of Sol's or Marty's most recent categorization?

Hearing nothing, then we proceed to a break now, is that right?

DIRECTOR DENTON: Are you going to assume now

that the -- my count is we have nine high chemicals, approximately 15 low chemicals in the low category and the rest are in the medium category.

So is the panel assuming that that's the prior -- do you need any further discussion or are you ready to go to public comment?

CHAIRPERSON MACK: I think the only meaningful discussion can be on a chemical-by-chemical basis. And so we had the opportunity for that.

So what we're going to do now is take a break. And if somebody wants to make a public comment, please submit us a piece of blue paper. And I have to go back on what I requested before, because I can't enforce your avoidance of all interpretation.

But I would just plead with you that we really want to get at the categorization itself and the judgment as to why you wish it to be changed.

Okay. We'll have a 25-minute break.

DIRECTOR DENTON: No. We'll have a 15-minute break and we'll come back at 11:25.

(Thereupon a recess was taken.)

CHAIRPERSON MACK: Let's begin. Before we start with the blue cards, something has been brought to my attention. And that is that I made the statement in the beginning that probably a matter of "when" rather than

"if" each of these chemicals or each of these compounds will be reviewed.

The question is whether or not, A, that's true and, B, whether or not it's true I have any business saying something as definitive as that.

And I probably have to admit that I don't. That's not my call. It's the call of OEHHA. And the call may be made in the far distant future as to whether some of these chemicals will ever actually be reviewed. We're in the job of prioritizing. And that means that we would prefer that the ones we give high priority to are the ones that are considered first, whether or not the ones at the end of the list ever actually get addressed.

And because it's not my call to say that, I would like to strike that comment from the record, and say -- I'll say it in some other way here, that because there is evidence of carcinogenesis in most of these, they should be considered for coming up before the Committee at some point, but it's not for me to say whether they actually will.

Although I would state my opinion that the ones that we call a high priority should come up relatively as soon as certain in the sequence.

Is that fair?

Okay. Now, where is Tim? Let me begin with the

people who want to comment on fluoride. We have limited time. We have designated fluoride to be high priority. As I look at the organizations that are represented by these 7 blue cards, I don't think there are any who want to decrease that prioritization to medium.

There are two who wish to do that.

Okay.

Then those are the two that I want to hear from, I guess.

You guys are really trouble.

(Laughter.)

CHAIRPERSON MACK: Okay. Jay.

Yes, Carol.

CHIEF COUNSEL MONAHAN-CUMMINGS: Dr. Mack, I don't know if you've mentioned it, but there does need to be a timeframe limitation on the public comments, especially since we have -- did you decide how much time you wanted to give people.

CHAIRPERSON MACK: Right. I requested, I think in the beginning, if I didn't, I meant to, that we would only be able to accommodate five minutes per comment. Most of the people who put comment requests down have suggested that they don't want to speak for much more than four or five minutes. But I'm going to try really hard to hold you to that.

So let's begin with Jay, who is going to have a comment on fluoride downgrade.

DR. MURRAY: Thank you, Dr. Mack and members of the CIC.

Thank you a second time.

I'm Dr. Jay Murray.

I'm speaking on behalf of the Consumer Healthcare Products Association. And I am going to put forth the argument for why fluoride should not be a high priority. Your background information indicated that there had been no authoritative body that had reviewed fluoride since IARC had done that in 19 -- I think it was 1987, and that is true.

What it doesn't say is that there was an extensive review by -- in 2006 by the National Research Council, Committee on Fluoride in Drinking Water, which was chaired by Dr. John Doull. And the conclusions of that NRC 2006 review, I'll just read you a couple of sentences.

On the epidemiology, their conclusion was, "The human epidemiology study literature, as a whole, is still mixed and equivocal." And on the animal studies, their conclusion was, "The collective data from the rodent fluoride toxicological studies do not present convincing evidence of an association between fluoride and increased

occurrence of bone cancer in animals."

So you do have a NRC 2006 review that you can rely on, even though that is not a Prop 65 authoritative body.

The public health benefits of fluoride are well recognized. Drinking water fluoridation is supported and endorsed by many organizations, including the Centers for Disease Control, and the U.S. Surgeon General. The American Dental Association has weighed in on the safety of fluoridation as well.

And, Dr. Mack, in your presentation, you had mentioned that there was a new study that had come along recently. And it wasn't clear to me which new study you were referring to. There's a study --

CHAIRPERSON MACK: The relatively new study was the one that occurred in 2006 by I think it's Bassin.

DR. MURRAY: The Bassin study.

Well, on the Bassin study, because there were two possibilities when you said that -- and I appreciate you clarifying that. The Bassin study was an epidemiology study done at Harvard as part of Dr. Bassin's Ph.D. thesis. And she reported an association between childhood exposure to fluoride from drinking water and osteosarcoma in males less than 20 years old, but not in females.

So this was a study that broke down into many

different groups. And the one group where they reported an association was males less than 20 years old. The epidemiology -- these studies, by the way, were based on --

CHAIRPERSON MACK: Jay, I'd prefer you didn't get into the details of the pros and cons. I understand your point. I think you've made it. You've made the point that there was a review and that that study may or may not be perfect. When we actually discuss fluoride, we'll go into that in great detail.

DR. MURRAY: I understand what you're saying, but --

CHAIRPERSON MACK: I'm saying no more time.

DR. MURRAY: No more time on Bassin. But what I want to tell you is there is a second newer study since Bassin by Douglas et al. also at Harvard.

CHAIRPERSON MACK: I'm aware of that.

DR. MURRAY: And that study says don't put weight on the Bassin study.

CHAIRPERSON MACK: Thank you. I appreciate it.

DR. MURRAY: And so, you know, I'd really urge you to consider the NRC. And to summarize, human and animal data are equivocal. Genotox conflicting. And I recognize you're not making a listing decision today, but you do want to have as high priority chemicals ones that

have a reasonable chance to be listed.

And if the NRC is correct that the data are equivocal, it's going to be hard for that compound to meet the clearly shown standard. Also, I urge you to consider the benefits --

CHAIRPERSON MACK: Thank you, Jay.

DR. MURRAY: Thank you.

CHAIRPERSON MACK: And is there a -- is it Dr. Pollick.

DR. POLLICK: Yes.

My name is Howard Pollick. Thank you for the opportunity to talk to you today.

I am a clinical professor at the University of California, San Francisco since 1981. I sit on fluoride committees with the American Dental Association, with the CDC, with the California Dental Association. I've already submitted my remarks in writing with the California Dental Association.

I just want to address four points. They may increase in number, but depending upon the time.

CHAIRPERSON MACK: Very little time.

DR. POLLICK: Very little time, I understand.

So my objection is over the prioritization criteria. The same standards should be applied, I believe, for all of the reviewers. And just because

something is widespread in its use or that there's a lot of studies did not lead all of the members of the Committee to come to the same conclusion on prioritization. And so that's a statement I wanted to make.

Second of all, it's important that the public be well-informed as to the meaning of prioritization and the interpretation of prioritization.

Does it mean that, in fact, this Committee believes that there is sufficient evidence of carcinogenicity from the studies that were reviewed? That's an important statement that needs to be made, because it's not clear to me, that based upon the criteria used in fluoride, that there is sufficient evidence, positive evidence, of carcinogenicity.

As has been eloquently stated by Dr. Murray, the IARC review indicated -- they gave it Category 3. The NRC review of 2006 is important. The University of York review of water fluoridation is important. And like I say, I've submitted many comments, and I don't want to go into the details of that, because I don't think this is appropriate at this particular time.

And, you know, if there's any further questions you have of me, I'd be happy to provide answers.

CHAIRPERSON MACK: I think it's fair to say, on

behalf of the Committee, that we do not feel that there is sufficient evidence of carcinogenicity. We do feel that there's widespread concern and that there hasn't been a formal review in the form of an authoritative body recently. And that such a review is probably appropriate at this time.

DR. POLLICK: If I may just add. I think that we welcome a review, because we feel that the evidence would show that fluoride -- inorganic fluoride is not carcinogenic and this would actually provide a lot of support for the use of fluoride and its use in water fluoridation, toothpastes, and dental products to prevent tooth decay.

CHAIRPERSON MACK: I agree that it would show that. So let's see what happens. We'll hope that, in fact.

DR. POLLICK: So it appears that the prioritization ranking will hold?

CHAIRPERSON MACK: I think, yes.

DR. POLLICK: Thank you very much.

CHAIRPERSON MACK: I know your point of view and you've expressed it, and you don't -- you're not in favor of changing the categorization.

THE COURT REPORTER: Can he identify?

MR. HIRZY: There are some pools in the

assessment that I'd like to point out if I may?

CHAIRPERSON MACK: Okay.

MR. HIRZY: My name is William Hirzy. I'm vice president of National Treasury Employees Union Chapter 280 at EPA headquarters.

There are -- under human data, there should be an X under the case series box. Under animal studies, there should be an X in the tumor initiation promotion or co-carcinogenicity studies. And there should be an X in the other relevant data box. Hormonal activity disruption and other mechanistic studies should also have an X in them.

And if I may make one brief rebuttal to Dr. Murray's comments --

CHAIRPERSON MACK: I really don't want you to do that. We just don't have time.

MR. HIRZY: Well, there is no Douglas paper. EPA is waiting for it and it doesn't exist. There's no peer-reviewed study that is --

CHAIRPERSON MACK: When the time comes undoubtedly we'll see it. Thank you.

CHAIRPERSON MACK: I'm sorry. I don't want to be rude, but this can go on for days. And I realize it's not your fault. It's our fault.

Now, I think we're done with the fluoride

discussion, because I think most of the other people who wanted to speak would be in favor of a high priority for review.

And I have heard nothing to change my opinion about whether or not there should be a high priority of review. I certainly don't think that means that we think that fluoride is carcinogenic at this time.

Okay, I'm being asked that I should let everybody speak.

So, Mr. Hirzy.

MR. HIRZY: Thank you. If I could just reclaim say three minutes. I presume I talked about two minutes before.

The fact that there is no Douglas Study I wanted to expand on that point. When I spoke -- the NRC recommended that EPA conduct a new risk assessment because their current drinking water standard wasn't protective of public health. It's been three years now since that recommendation went in.

When last I spoke to the Division Director, Ed Ohanian at EPA, and asked him where is that risk assessment, he said we're waiting for the Douglas paper. Now, what that tells me is that EPA is on the horns of a dilemma. If nothing refutes the Bassin epidemiology study, EPA is going to have to find fluoride to be a human

carcinogen, which means MCLG 0 and the end of the water fluoridation program.

So EPA basically is waiting for some excuse not to find EPA -- not to find fluoride a human carcinogen. If it's going to happen, it's going to happen by the good graces of the civil servants in California. It is not going to happen in D.C.

And so I just urge you to take a look at the age-specific exposure data on Epi studies that have not found an association so far, which is what Bassin did, which was the magic in finding the link.

CHAIRPERSON MACK: Thank you, Mr. Hirzy.

All right, David Kennedy.

DR. DAVID KENNEDY: Yes, I'll just take a second.

You were furnished by Dr. Thiessen who was on the National Academies and not the National Research Council. Some people are calling it National Resource. It's Research. And that she furnished you what their committee said.

They basically said that -- they didn't say it was a "frank" carcinogen, but they did not consider whether there was insufficient information on -- clearly not carcinogenic was not applicable. And so the most recent review is someplace in the medium range.

And she mentioned this document. This has been

through a whistleblower lawsuit. It was written by Dr. William Marcus, who is a Senior Science Advisor, Office of Drinking Water. And in there, he goes through in detail why you have to consider the in vitro studies. It's required by law. And they want to use, and you have had submitted to you the Ames test. And he quotes a letter from Dr. Ames to Upjohn saying it's not applicable to fluoride. It's not an adequate agent. It's not an adequate test. You need to look at the other tests. All of them come out positive, sister chromatid exchanges, mutagenicity.

That, plus in here, he took the 6,000 control animals and showed that they actually were a medium-dose animal, based upon the amount of fluoride in their legs, bones, and --

CHAIRPERSON MACK: Please, please, please. All of this is pertinent. All of it is pertinent to a discussion of a listing, not for just a list of prioritization.

DR. DAVID KENNEDY: When will that occur?

CHAIRPERSON MACK: Well, we don't know, because we haven't gone through the remaining batch of chemicals. It's not for me to say. All I can say is we have made a decision about prioritization and it will occur sooner rather than later.

DR. DAVID KENNEDY: Well, I understand --

CHAIRPERSON MACK: And it doesn't make any difference. It's not today. And there will be adequate time for this kind of discussion then.

DR. DAVID KENNEDY: Let's hope so. But one thing that has remained to be mentioned is that when we're talking about exposure levels, the rats that drank 79 parts per million fluoride had dysplasia of lip, tongue, throat, cancer of the bone and cancer of the liver. Dentists are painting 50,000 parts per million fluoride in children's teeth in an application called varnish. And dentists are applying 15,000. So where the rats overdosed or underdosed?

CHAIRPERSON MACK: Thank you, Mr. Kennedy.

DR. DAVID KENNEDY: Dr. Kennedy.

CHAIRPERSON MACK: Dr. Kennedy.

Danny Gottlieb.

MR. GOTTLIEB: Good morning. Thank you all for being here and doing the job that you feel is necessary. I'm Danny Gottlieb. I'm a 71-year old retired food scientist and agriculturalist having worked in those areas.

I want to talk mainly about, for a couple minutes, about critical mass in fluoride exposure. And I submitted a chart earlier, which in considering --

following up on what you've said, we need to consider exposure. Considering the exposure that I want to use an example, one child that represents hundreds of thousands in California going to -- just getting up in the morning and not having enough food going to school and having the breakfasts that the school gives. And then you have grape juice, the grapes were sprayed with the cryolite pesticide -- fluoride pesticide. And then eating pancakes and the pancakes were -- the grain was fumigated with sulfuryl fluoride.

And then that morning they do not brush their teeth. In this particular town, they don't have fluoride in the water. But through the day, the child is accumulating this fluoride in the meals. The raisins were sprayed with cryolite that they have in the school lunch, and on and on. I won't get into detail.

But I'll summarize by saying or reading, "According to the World Health Organization in combination with certain other factors, sub-optimal nutrition, kidney disease, a chronic fluoride intake of between two and eight milligrams per day can produce the pre-clinical stages of skeletal fluorosis."

What's happening is that you must consider not just one application of fluoride, you need to look at the critical mass of all the things that the children are

getting in the schools. And it's going to wind up in crippling skeletal fluorosis. And who knows yet how much -- and this all starts in kindergarten.

There's a new California law that says --

CHAIRPERSON MACK: Mr. Gottlieb, we really can't go on about other things than cancer. And I don't think you want to -- I don't think you want to change the categorization. I just need you to stop now.

MR. GOTTLIEB: Okay. I understand your constraint. I've submitted my packets and I hope you study them and come to the right conclusions.

CHAIRPERSON MACK: Thank you.

MR. GOTTLIEB: This is a once-in-a-lifetime chance to let the people that can do something about it make the right decision.

Thank you very much.

CHAIRPERSON MACK: Thank you. Renée Sharp.

MS. SHARP: So I'll be really brief, because I know that you know that we agree with your assessment.

But I just wanted to say a couple words, because Dr. Richard Clapp, who is a professor at the Boston University, School of Public Health was not able to actually send his comments to you all in time and could not be here today.

So I just wanted to read a couple of sentences

that he wrote in his comments that is applicable to when you actually do look at fluoride in the future, which is that, in general, he agrees with the National Research Council's assessment of the epidemiological literature. And notes that the most recent studies have included much more focus on an individual level, of exposure estimates. These studies should therefore be given more weight than earlier group studies that failed to examine age and sex specific associations between fluoride exposure and osteosarcoma. He's also important to note just because we had someone else coming up and speaking about why that's not important.

So thanks.

CHAIRPERSON MACK: Thank you.

Chris Neurath.

MR. NEURATH: Yes. I'm Chris Neurath or Neurath, the American Environmental Health Studies Project.

I will -- anything that I submitted in writing, I won't repeat. But I'd note that the funding for OEHHA to do these assessments is not unlimited. And so even though, I agree that high is the right category, I'd like to encourage you to do as high as possible, because if you have five that are high, you may not get to number 5. So this -- I know it's something the panelists said. We want to make it medium to high, so I'm saying high plus.

You also said that if there was new exposure information or studies, that you hadn't considered, that this would be an appropriate time. I'm not going to discuss the exposure. I submitted that all in writing, but it's basically fluoride exposure is ubiquitous and unavoidable, including at high levels, 48 percent of kids in fluoridated areas have dental fluorosis, which is a sign of over exposure.

As far as cancer, I do have additional information, which is one slide that in -- and we can move to it.

CHAIRPERSON MACK: We really can't do slides. We just don't have time.

MR. NEURATH: It's already set up there. But this is from Dr. Vyvyan Howard, Centre for Molecular Biosciences, University of Ulster in Ireland, Northern Ireland. He's a toxico-pathologist specializing in the problems of toxic substances on the fetus and the infant. And it's slide number 4 or 5, if you -- it's the one with micrographs. I won't go into all his qualifications.

(Thereupon an overhead presentation was presented as follows.)

MR. NEURATH: But, yes, this is the one.

You have the category of evidence of genotoxicity, mechanisms and other. This is a other or a

new way of looking at cancer tissue dysgenesis. And I will paraphrase from his couple sentences from what he says.

It is widely recognized that congenital malformations carry an increased risk of cancer. However, they're generally observed naked eye and do not involve a histological appraisal for them to be recorded. Tissue dysgenesis, a condition that is not usually detectable by the naked eye, but which requires microscopy, can also be associated with an increased risk of the development of cancer.

And he mentions several cases, other types of cancer and things, testicular dysgenesis syndrome is a classic one.

The relevance of tissue dysgenesis to the association between fluoride and osteosarcoma concerns the appearance of bone tissue following high fluoride exposure. The photographs up there are photographs of bone -- animal bone, which he says revealed a frankly dysgenic appearance.

Although, it can be argued that this was a high dose experiment, the effect of lower dose exposure to fluoride, on a three-dimensional spatial arrangement of bone, has not been widely investigated. As mentioned previously, quite subtle degrees of tissue dysgenesis in

other systems have been associated with increased cancer vulnerability.

So basically, he believes this is another marker supporting the osteosarcoma or bone cancer linked to fluoride.

CHAIRPERSON MACK: Thank you, Mr. Neurath. I think that's probably enough. We get the message.

Jeff Green.

MR. GREEN: Yes, Doctor. For the record, My name is Jeff Green. I'm the national director for Citizens for Safe Drinking Water. I'll be very brief. I don't really want you to change the prioritization.

My concern would be is if this procedure is followed through, is that you eliminate all advocacy and whether it's from one side or the other and that you take it from a strictly straight line, which is very difficult to do obviously.

But my main concern would be is that the primary purpose of Prop 65 in the first place was to inform and warn people obviously. And unfortunately, we get into the fact about whether one person agrees or doesn't agree. There's always somebody with a product that doesn't really want that to happen. But I have to say that the specific chemical or the specific thing that gets put in, not only in the water, but in other places, unfortunately it also

has a sales tool out there that tells everybody it's the greatest thing in the world.

And so there's a concept called sophisticated user. That basically has to do with the fact whether somebody can protect themselves. And so why I believe that the process you're going to go through is extremely important. And I'll end it with that.

Thank you very much.

CHAIRPERSON MACK: Thank you.

Jeanette Bajorek.

MS. BAJOREK: My name is Jeanette Bajorek. I live here in Sacramento on the edge of Carmichael. The Sacramento Suburban Water District has just fluoridated my water, which means I pay their bills, but I can't drink their water. I can't eat the apricots in my backyard. I can't plant a garden this year, because everything is polluted with the sprinkling water.

But that's nothing compared to the youngsters who live in some fluoridated areas and are coming down with osteosarcoma. This is a very, very painful disease. The drugs don't reach it. Pain killers don't reach it. There's no escape from the pain. But now there's if -- and then they have to endure, what do you say, cutoff the limbs. They have to endure that also before they finally die from the disease.

If there's one bright-eyed tousle-headed kid anywhere in the world who has to die this way, just because their neighborhood was fluoridated, then I think that's reason enough to ban it from the waters in California.

CHAIRPERSON MACK: Thank you, Ms. Bajorek.

All right. Now let's move to people who want to change the category.

Stan Landfair from DuPont. We've got three people from DuPont, each of whom wishes to speak about PFOA. Do we really need three, Stan?

MR. LANDFAIR: Yes, we do. But I can promise you we'll be very efficient and very brief.

CHAIRPERSON MACK: All right.

MR. LANDFAIR: Okay, thank you.

And, yes, for the record, I'm Stanley Landfair, law firm of McKenna, Long & Aldridge representing DuPont.

I just need to address some process questions before my clients will address the substantive questions.

The first one, kind of -- I need to ensure that our written comments have been distributed to the panel and to the staff. Okay.

And now having asked that, the reason for asking was because in the OEHHA -- I presume it was OEHHA who prepared this handout that was on the table. There is a

blank in the column for new studies.

And in our comments, we did bring to the agency's attention that there are two new recent studies submitted regarding PFOA, both in 2008, one which is an EFSA scientific review, which is an epidemiological study which concludes that negative findings for four different suspected types of cancer that have been addressed here.

And the other is a more recent Danish cohort study on the issue of exposure that indicates that exposure is decreasing and decreasing very rapidly.

So the other process point I need to ask is, our clients will be brief, but will you entertain the question of downgrading the priority? There is so much that we find we agree in the oral analysis of the data and it strikes us that, in our opinion, if we can say so, that the proposed priority over-emphasizes the issue of exposure versus the fundamental question of whether or not the data would support listing in the first place.

PFOA is not a new question to this panel. It's not a new question to other federal agencies that have looked at it. And other agencies, like the EFSA and the Danish cohort -- it's not just the trend, it's the overwhelming conclusion that the existing data simply would not support a finding that it should be listed. So we just need to ask you in all earnestness, if you're

intent on reviewing it, would you please just hear us out on why we think it should be downgraded in priority, and we will be extremely brief.

CHAIRPERSON MACK: David Boothe.

DR. GERALD KENNEDY: Yeah. My name is Jerry Kennedy and I'm a toxicologist with the DuPont company. I retired April 1st, April Fool's Day. So that probably tells you all you really need to know.

But I'd like to just take a minute and review the facts. And Dr. Eastmond pretty well stated the facts. This is an unusual situation, where we do have human information to review, specifically with cancer, and looking at the populations of people that have made and used this chemical both at the 3M Company and then our company. The cancer rates appear to be background noise and no more. And that data is pretty solid. It covers 4,000 people at 3M that have worked with this material since the fifties. And it covers about 6,000 of our people that have worked with it about the same period of time.

There's no question they've been exposed. And it looks like the playback is favorable and that there is not a cancer threat for following those exposures.

The Erickson study that was just mentioned looks at background populations. They looked at -- or they had

recruited something like 57,000 people back in the mid-nineties and followed those folks for cancer. And they found roughly a thousand of those have developed cancer by the year 2006. And those cancers -- all of those folks had their PFOA levels measured. And the people that had cancer versus those that didn't have cancer in those populations, the PFOA levels were exactly the same. So it doesn't look like there's an association between cancer and that population and PFOA exposure. So the human data looks pretty good, as good as can be expected.

The word inconsistency just pops up I think when you see 50 or 60 different endpoints, and some move up and some move down.

The animal data, it's true that one species, one sex does respond. The responses are benign adenomas of three tissue types, the testes, the pancreas and the liver. PPAR-alpha seems to be a mechanism that's operative here. With 11 pharmaceuticals that act on the PPAR-alpha receptor, when they're tested in this rat strain, seven of those produced this exact same tumor triad. And all of those drugs apparently are free of cancer risks, as we know it today. So it looks like the animal information is telling us that, yes, they can respond, but that the mechanism of response might not be

human relevant.

And thirdly, the material appears to be non-genotoxic. There's a wide variety of studies that have been done, both routine-type studies and experimental research-type studies. And then the main, when you look at the weight of evidence, this does not seem to be a genotoxic material.

So, I mean, to conclude that we think there's a -- and I didn't mention, but the database for this chemical is great. You complained about three-ringed notebooks, well I have a collection of them too. There's a lot of paper. There's a lot of information, but I think it's pretty consistent that humans don't respond. The animal data is one sex of one species. Female animals don't respond non-genotoxic. And the mechanism of action, the PPAR-alpha activation, appears to be not particularly human relevant. So we didn't think there's much information here to support listing this material as a carcinogen.

CHAIRPERSON MACK: Thank you, Mr. Kennedy.

Mr. Boothe.

MR. BOOTHE: Dr. Mack, Dr. Denton, members of the Committee, thank you for agreeing to allow us to speak. I will be brief. My name is David Boothe. I'm with DuPont Company. I'd like to persuade you against a high or

medium priority for PFOA, its salts and precursors. We find ourselves, as you heard Stan Landfair and Dr. Kennedy describing, in fair agreement with the assessment of the science you heard Jerry Kennedy's summary there of our views. But we do respectfully disagree with your conclusions for a medium to high priority or ultimately high priority.

A general concern, absent data that clearly supports a priority, does not argue for a high or an even medium priority. As we outlined in our comments, general exposure is clearly declining at a rapid pace per the NHANES data and the CDC, as well as the New York State study that's cited and other data. Particularly, there is a new study that just came out within the past month indicating a constituency in Norway, where we see similar declines.

That's attributed by the U.S. Environmental Protect Agency to a PFOA stewardship program, that all major players in industry are involved with to reduce emissions, product exposure, and ultimately to go to phaseout of these types of materials.

We would ask that the Committee consider whether you see that there is a real risk here that justifies further evaluation at all and the expenditure of resources needed compared to other priority items that you may have.

So we respectfully ask that you reconsider your position, categorizing the priority instead to a low priority level, that we believe is fully justified by the data and the science. And further, by the clear evidence of declining exposure in the population to the stewardship activities taking place.

Those are my comments. And I do thank you for the opportunity.

CHAIRPERSON MACK: Thank you, Mr. Boothe.

MR. LANDFAIR: Just to return to a point of process. If I can ask for the benefit of everybody, how do we intend to proceed from here? Is there going to be a vote at the end of the --

CHAIRPERSON MACK: I think the sensible thing to do, rather than interrupt each time, is to wait until all of the comments have been made and then the Committee will discuss whether or not we want to change any prioritization.

MR. LANDFAIR: That's fine.

Thank you very much.

CHAIRPERSON MACK: Sarah Janssen.

DR. JANSSEN: I'm not speaking on fluoride.

CHAIRPERSON MACK: Pardon me?

DR. JANSSEN: I'm not speaking on fluoride.

CHAIRPERSON MACK: No. We're long finished with

fluoride. You're speaking on many things, but not fluoride.

DR. JANSSEN: I'm so sorry.

I'm trying to do too many things at once. Good afternoon. My name is Sarah Janssen. I'm with the Natural Resources Defense Council, where I'm a physician and scientist. I also have an Assistant Clinical Professor position at the University of California, San Francisco, in the Division of Occupational and Environmental Medicine.

And my comments are about the PPAR-alpha mode of action, which we've already heard about once this morning. I think this is relevant not just to PFOA, but to a number of other chemicals under consideration, including DINP, triclosan, and the -- my comment is that a new study, which was just published, on May 15th in Environmental Health Perspectives, which discusses whether or not PPAR-alpha is a relevant mode of action for understanding the relevance to human carcinogens.

And the conclusion of that study, which is available free to everyone on-line, is that PPAR-alpha alone is not a sufficient mode of action for causing cancer, and that there are probably other relevant molecular pathways that result in hepatocarcinogenesis, and that we shouldn't dismiss PPAR-alpha as a mode of

action not being relevant to human cancer.

So that's my comment on PFOA. And if you will take into consideration for also triclosan and DINP, I don't have to come up again and speak.

CHAIRPERSON MACK: I think all of those comments for each chemical is highly pertinent to the discussion of listing.

DR. JANSSEN: Okay.

CHAIRPERSON MACK: Whether it's a major player in the discussion of prioritization is another matter.

DR. JANSSEN: So I'll come back and speak again.

Thank you for your time.

CHAIRPERSON MACK: Thank you.

Lisa Navarro.

MR. LIVINGSTON: Dr. Mack, with respect to triclosan, do you want to do that now or do you still want --

CHAIRPERSON MACK: Yeah, we can do that now.

Whoever wants to go first.

You're Lisa Navarro, I gather.

DR. NAVARRO: Hi. I'm Lisa Navarro with Ciba.

Thank you for your time. I'd like to just read one statement in response to the comments on the Guyton publication. This is specifically a comment from the Chief of the Pharmacokinetics Branch from the U.S. EPA, in

which he says, "I think the Guyton paper describes the mode of action for DEHP, but does not provide insight into PPAR and tumors in rodents versus humans. One of the difficulties in environmental tox is that the chemicals are biologically dirty. That is, they most likely have multiple actions in a biological system.

"In contrast, drugs such as triclosan, have been designed to have as few, preferably one, biological action. Thus, DEHP has actions independent of PPAR that lead to liver tumors in rodents. This does not negate the hypothesis that PPAR activation in rodents leads to liver tumors and that these tumors are not relevant to humans.

"In fact, the DEHP example cannot support nor refute this hypothesis, since DEHP has actions that led to liver tumors independent of PPAR."

CHAIRPERSON MACK: Thank you. Gene.

MR. LIVINGSTON: Pull my card.

CHAIRPERSON MACK: Pull your card. Okay, I'll be happy to pull your card.

MR. LIVINGSTON: Thank you.

CHAIRPERSON MACK: Derek Gammon?

DR. GAMMON: Hello. I'm here to discuss permethrin. First of all, thank you for the panel and for OEHHA reviewing the permethrin toxicology package.

I'm a staff toxicologist -- sorry, I'm a Senior

Toxicologist at FMC Corporation, who are the principal manufacturers of permethrin. I previously spent 16 years working for DPR in this very building doing risk assessments on pesticides.

The first point I'd like to make -- there's two points really. The first point is that we believe that you are incorrect, Joe, in claiming that there was an increase in malignant tumors with permethrin in the mouse. But in all five studies -- three of those five studies showed an increase in either lung or liver adenomas, but not in carcinomas. It's non-genotoxic.

The second thing is that we have some preliminary data, which suggests from a mode of action standpoint, that the mechanism is liver enzyme induction, P450 induction. And we have set up some experiments, which are going to be conducted in the future to nail this one down. And we firmly believe that when we've done these studies, that permethrin will be reclassified as a rodent-specific non-genotoxic carcinogen. So we'd humbly request that you remove it from medium to low.

CHAIRPERSON MACK: Thank you.

Annette Shipp.

DR. SHIPP: I have no further comments to add. I agree with the review of Dr. Landolph.

CHAIRPERSON MACK: Thank you.

Jay, do you want to discuss aspartame?

DR. MURRAY: Sure. Thank you. I'm Dr. Jay Murray. I'm speaking on aspartame on behalf of the Calorie Control Council.

And Dr. Landolph made the presentation on aspartame and said that he was on the fence between a low and a medium for aspartame, and shaded up to medium. What I'm going to try and do is urge you to consider shading the other direction from medium down to a low on aspartame.

And the basis for that is that the background materials that you received said that there were no authoritative bodies that had reviewed aspartame. And I want to correct that. The Food and Drug Administration, which is a Prop 65 authoritative body, definitely reviewed the carcinogenicity of aspartame.

You know, they went through this several times back in the early eighties when aspartame was first approved. And most recently, FDA has taken another look at the potential carcinogenicity of aspartame as recently as April of 2007.

And I won't spend the time to do this, but the written comments that I submitted has the quotations from FDA from their most recent 2007 review of carcinogenicity.

There's another authoritative body that has

weighed in on aspartame as well, and that's the National Toxicology Program. There are three NTP transgenic mouse studies of aspartame that have been reported in the last five years. And all three of those studies were negative. So you have not one but two authoritative bodies that have recently expressed an opinion on aspartame.

Also, there are -- there's no shortage of studies. There are a lot of epidemiology studies of aspartame, but they are not positive studies. There are lots of animal carcinogenicity studies of aspartame. There are seven negative carcinogenicity studies and two more carcinogenicity studies that are scientifically inappropriate, unconventional studies, which have been the subject of a number of peer reviews by others.

There is one additional piece of new information. Four days after the deadline for written comments, there was a paper by Schoeb et al. that was published in veterinary pathology. And the significance of that paper -- I'm not going to go through all the details of that study. But the significance is the authors concluded that it is more likely that what the authors of the Ramazzini Studies interpreted as lymphoma was not, in fact, cancer at all. That it was pulmonary lesions related to a rampant infection of mycoplasma pulmonis going through the rat colony. And if you look at the

incidence of broncho pneumonia in that study, it was as high as 97/98 percent.

So you got seven negative studies and two really bad studies, where it's questionable that they were really seeing cancer when they were calling it as cancer.

So for those reasons, I won't take anymore time. I would just encourage you to think about, you know, do you really want to shade up to a medium or would it be more appropriate to shade down to a low, given that information.

Thank you.

CHAIRPERSON MACK: Thank you, Jay.

Fernando Suarez.

DR. SUAREZ: Good morning. My name is Fernando Suarez. I am a toxicologist. I work for Syngenta Corporation.

I just wanted to state that I agree with your evaluation of our two products, thiamethoxam and benoxacor. The only comment I wanted to make sure to voice here is that during the presentation of benoxacor, there was a list of crops that were mentioned as a possibility that these products used. And although that's, in fact, in the label of some of the products, for benoxacor specifically, there is no economic benefit in any of these crops, except for corn. In other words, the

only crop that we know for sure for certain that is benoxacor's use is corn.

Other than that, I would like to make myself available for any questions you may have and I thank you for the time.

CHAIRPERSON MACK: Thank you.

Robert Barter.

DR. BARTER: Good afternoon. My name is Robert Barter. I'm a toxicologist with ExxonMobil Biomedical Sciences. And I'm here today providing comments on behalf of the ACC Phthalate Esters Panel.

I'd like to try to persuade you to move the prioritization of diisononyl phthalate from high to medium. In Dr. Eastmond's description of the available data for DINP and its prioritization as a high, he indicated he had concerns in regards to exposure, as well as in the tumor data available from animal models.

In regards to the exposure, first, I'd like to point out that DINP is no longer used in toys that can be placed in the mouth for children. This is done by legislation in the State of California, reducing that potential exposure.

Additionally, the Consumer Products Safety Commission of the United States convened an expert panel in the early 2000's to evaluate risk of DINP exposure To

children from the use of toys. If my memory Is correct, OEHHA participated on that expert panel. They considered childhood exposure to DINP and cancer risk and determined that there was no risk from cancer from exposure to DINP in toys.

Finally, there's extensive biomonitoring data available on diisononyl phthalate looking at urinary metabolites of DINP. What has been found to date through the NHANES database and the Centers for Disease Control is that 75 percent of the human population, both adults and children, have non-detectable limits of detection for DINP in the urine. And secondly, when exposure is detected, the exposure is exceedingly low.

In regard to tumors observed in animal models, three tumor types were listed. All three of these tumor types have been determined to be of no relevance to humans in cancer risk assessment by various authoritative bodies.

Specifically, liver tumors observed in rodent liver. Liver tumors observed in rats and mice for DINP do work through peroxisome proliferation mode of action. It's the only mode of action that's been established for DINP in terms of liver tumor development.

The DINP meets all the criteria identified by both IARC as well as ILSI in terms of establishment of human relevance for these liver tumors.

As Dr. Eastmond noted, there is suggestive evidence through a paper published in 2007 that indicates DINP -- or excuse me DEHP can induce liver tumors in PPAR-alpha knockout mice.

What's also known is that there's a high spontaneous rate of liver tumors in these PPAR knockout mice. And the postulated mechanism by the authors of the paper Ito et al. indicated that there was likely an increase in oxidative stress observed in these mice that led to liver tumor development. In any study done with DINP, there's been no observation of increased oxidative stress in the liver.

Two other tumor types, the male rat kidney tumors that were observed following DINP exposure, have been deemed not relevant for human cancer risk assessment. This is the alpha-2u-globulin mechanism. And DINP meets all the criteria identified to indicate that this mechanism -- or this mode of action isn't i-n place.

And in addition, the leukemias observed in the Fischer 344 Rat are considered to be of no to little relevance to humans by numerous authoritative bodies, including EPA, NTP, IARC and the Consumer Products Safety Commission.

In fact, NTP has moved away from the Fischer 344 rat due to the high spontaneous rate of these leukemias

observed in Fischer 344.

Finally, I would like to touch on one last comment that was made that EPA had expressed some concern for DINP in terms of cancer potential. This was done through a federal register notice in 2000, in which DINP was under consideration for the Toxic Release Inventory. In 2005, after public comment was received, EPA revised and reserved judgment on the cancer issue for DINP.

And we think that this data -- this information taken in total should reduce the prioritization of DINP from high to medium and potentially low.

Thank you for the time.

CHAIRPERSON MACK: Thank you, Mr. Barter.

Gary Van Riper. Is it Ripen?

DR. VAN RIPER: Van Riper.

CHAIRPERSON MACK: Van Riper. Got it. I don't know of any other Van Ripers. I know some Ran Vipers.

DR. VAN RIPER: Well, it's a Dutch derivative way back. Thank you.

Dr. Mack and panel members, I appreciate the opportunity to talk to you. My name is Gary Van Riper. I represent the International Molybdenum Association. And I'm here as a member of the industry. I've had 34 years of work in the Molybdenum industry. I'm not a toxicologist. I'm an engineer. I'm here to talk about

exposure.

You mentioned there are two considerations that were important. One of them was the prevalence and the other one, the intensity. So I want to talk through those to give you a sense of molybdenum trioxide, and that's the chemical we're interested in.

From an involuntary exposure standpoint, we're not aware of any consumer use or products that contain molybdenum trioxide. It's a high-level intermediate that does not make it down to the consumer level.

Moly, as we call it in the industry, Moly is found in your house, in your stainless steel flatware and so on. So it is found prevalent across the country, the world. But it is in the alloy form. It's not in a trioxide form. It's in a zero valence. It's mixed with other metals, stainless steel. So there's really no exposure to consumers in the state from molybdenum trioxide. From a voluntary contribution or occupational exposure level, first of all, the product tested by NTP, there is no sale of that material in California, zero. Further, there's only one facility in California that uses Moly trioxide. It's a different chemical production process. It's a catalyst fabrication plant. And they use it in a wet process. So basically the drums or bags of material come in, are dumped into mixers and added water

and then they go through and they're pelletized in a catalyst form. So basically, there's very, very little exposure to any kind of trioxide, even in this one facility.

This facility meets exposure levels that are 1/100 the level of the lowest dose that was tested by NTP, 1/100. So we have minimal exposure on the industrial side, on the occupational side and really no exposure on the consumer side. So we would request that it be moved from medium to low, simply based on lack of exposure.

And one additional point that I think is very interesting is, and we pointed it out, but the NTP study took a product -- and I say this was 1/100 of the level that actually received by NTP. NTP further took that product and micronized it to a level of 1.5 microns. So all of the material they tested was 1.5 micron, which makes it 100 percent respirable. The material that they received is only .15 percent respirable. So they increased the respirable fraction by 600 plus times into the mice that were tested.

If you translate that back to the facility in California that makes catalysts, it's thousands of times different.

CHAIRPERSON MACK: Thank you, Mr. Van Riper.

DR. VAN RIPER: Thank you.

CHAIRPERSON MACK: I would propose that -- I will try and read the list of chemicals that have been commented upon. That each of the people who has reviewed those chemicals, we'll take a 10-minute break and ready --

CHIEF COUNSEL MONAHAN-CUMMINGS: Dr. Mack, I don't think your microphone is on.

CHAIRPERSON MACK: Pardon me?

CHIEF COUNSEL MONAHAN-CUMMINGS: Your microphone is not on or we can't hear you.

CHAIRPERSON MACK: I'm sorry. My microphone is on but my mouth wasn't close to it.

I would propose that we take a little bit of a break, so that each of the people can consider whether or not they want -- well, now it's on.

Each of the people on the Committee can consider whether or not they want to change their categorization proposal. And then we will speak to each of the chemicals quickly.

Does that sound all right, Carol?

CHIEF COUNSEL MONAHAN-CUMMINGS: That's fine, as long as the Committee isn't going to discuss that with each other. It's just a thought process of your own, right.

CHAIRPERSON MACK: Pardon?

CHIEF COUNSEL MONAHAN-CUMMINGS: So don't talk

amongst yourselves.

CHAIRPERSON MACK: Yes. No, no, no, don't talk among ourselves. Everybody -- everything is open here. It's bad, but it's open.

(Laughter.)

CHAIRPERSON MACK: Does everybody need a few minutes or is everybody happy right now?

MS. SHARP: Can we just note something. There were some of us who had actually written down several chemicals on our cards. And since you aren't going through chemical by chemical, we actually haven't gotten a to chance --

CHAIRPERSON MACK: Would you like me to read the names of the chemicals, is that what she is saying?

MS. SHARP: No, we're saying there may be a few more comments.

COMMITTEE MEMBER EASTMOND: She has comments on other chemicals.

DR. JANSSEN: I had other comments to mention.

MS. SHARP: I'm sorry. I'm Renée Sharp from EWG.

CHAIRPERSON MACK: If you wish to, please come up and do it.

MS. SHARP: I also wanted to give other people the opportunity. So I had been talking about fluoride, because we're talking about fluoride. But I also just

wanted to note that in PFOA, I'd just want to talk for a second, because I agree with your prioritization of PFOA and DINP. But I do want to make one comment on PFOA, because you did mention that the EPA Science Advisory Council -- Board, sorry -- had done this draft likely carcinogenic recommendation.

And then you sort of discounted it, because it was only draft. And I just wanted to point out that that may not be quite fair, considering how slow the EPA is.

CHAIRPERSON MACK: You're looking at me and I didn't do that.

MS. SHARP: I'm looking at all of you.

Thank you.

COMMITTEE MEMBER EASTMOND: I am the one who did that.

DR. JANSSEN: And I'm sorry. I wanted to make a couple other comments. My name is Sarah Janssen. I'm with the Natural Resources Defense Council.

First, on diisononyl phthalate or DINP, I wanted to make a couple of points. One, there was a publication by Silva et al., which is another group affiliated with the U.S. Centers for Disease Control. They did a follow-up study for looking at biomarkers of DINP exposure in 2006. It was published in Environmental Health Perspectives.

And in that study, which is not listed in your recent studies, they found a subset of the population, which was essentially adult men, when they looked for a different metabolite than they looked for before, it was an oxidative metabolite. They looked for three different ones and they found them in over 97 percent of the people in that study. These were not children. They weren't sucking on rubber ducks or pacifiers. These were exposures from sources that we don't understand, but we know that there is widespread exposure to this chemical.

And then I'll just reiterate that the Guyton et al. paper looking at PPAR-alpha agonist, identifying DEHP, will also apply to DINP. We're not asking you to make a decision about whether PPAR-alpha is a relevant mechanism. We're asking you to make a decision about prioritizing a chemical. And I would just urge you not to dismiss prioritizing it based on a mechanism which has now been shown to be probably not relevant to humans, but is also not relevant to the development of cancer in animal models.

The other chemical that I wanted to comment on is a different chemical. It's the chlorinated flame retardant TDCPP, which I think you ranked as being of a medium priority. I wanted to urge you to increase the prioritization for that chemical for several reasons.

One is TDCPP, if you may all remember, in 1977 was banned from children's pajamas, because it was found to be a carcinogen. It was identified by the Consumer Products Safety Commission as being, at that time, mutagenic in bacteria.

Since then, the chemical wasn't banned from production, it actually has found its way into our furniture foam and the textiles that are used in carpeting and curtains and other upholstery. It's actually being used as a replacement for the polybrominated diphenyl ethers, which have been banned in California and voluntarily removed from production in the U.S.

This chemical is a high production volume chemical produced in greater than a million pounds per year. There's likely to be high exposure to it in the population. And the Consumer Products Safety Commission in their recent review have identified this as likely carcinogenic to humans.

It is also quite structurally similar to other chlorinated flame retardants, which are already on the Prop 65 list identified as carcinogens, that's tris and TCEP.

And I just wanted to make one final comment about triclosan. And I just wanted to note again that I think that chemical, because of the PPAR-alpha question and also

because of the widespread exposure in the human population should be increased in priority. Again, the U.S. Centers for Disease Control biomonitoring data has shown that in the general U.S. population over 75 percent of us carry residues of this chemical in our bodies. And we need to have a better understanding of its toxic effects.

You guys are poised to make the expert decisions and direct our OEHHA scientists to conduct a thorough review of the literature that exist.

Thank you for your time.

CHAIRPERSON MACK: Thank you, Sarah.

Are you ready, Joe?

I'll start and then I just want to know if you need a moment.

COMMITTEE MEMBER LANDOLPH: Yeah, sure I can do it.

CHAIRPERSON MACK: Okay. I'll speak to the two that I've been assigned.

The first one is fluoride. You can already tell that I don't think I should change the prioritization, but that does not by any means mean that I know what the answer is going to be.

I just think because of the concern and because of the widespread exposure, it's reasonable to review it for the group.

The second one is molybdenum trioxide, which I actually was convinced by Mr. Van Riper that it should be downgraded from medium to low, on the basis of the low prevalence of exposure.

So I'm changing my categorization of molybdenum trioxide to low and keeping the categorization of fluoride to high.

So who'd like to go next? Are you ready, Joe?

COMMITTEE MEMBER LANDOLPH: Yeah.

So the comments on aspartame, which I think Jay and others have made. I struggled with this one. I mean, when I said medium-low, I'm one of these people who likes to use numbers. And I always split the categories. And when I sit on study sections, I do the same thing.

So, I mean, the best I could do -- I agree with all -- many of the comments that Jay made. And I know there's a lot of criticisms of Ramazzini studies. However, I've got to point out that before these guys who did this study, there was Maltoni and they did studies which were criticized on benzene, and they were absolutely right. So I'm a little bit hesitant to throw data into the hopper unless I'm sure.

So the best I could do is -- you know, I struggled between medium and low, and so I would say to OEHHA, and go against Joan's direct orders, place it at

the bottom of the medium category. I think that's about the best I can do. I can't -- I don't want to change it to low, because there's a lot of human use and I think it should be looked at. I'm not wild about looking at it immediately, but I still think it eventually should be looked at. So that would be the best direction I could give to you as an advisor.

What was the other one, Tom, was triclosan was next?

And there was a request to upgrade that from some very articulate comments from one of the speakers. And I looked at that very carefully. I'm concerned about it, because I teach microbiology and that's another whole discussion. But there's no epidemiology studies. The animal studies are negative in the rat, all the way up to 3,000 parts per million. They're negative in the hamster. The studies in mouse gave positives in liver for males and females. And that data was dose dependent for adenomas for carcinomas and for combined.

Sorry, same problem again. Thank you.

And the EPA said it was not likely to be carcinogenic to humans. Yes, there's a lot of human use. And there was a lot of discussion about PPAR-alpha again. And I struggled with this one. And I'm concerned about the human use, but I'm just not overwhelmed by the

carcinogenicity data.

So I think I'm going to say thank you to the speaker and, I respect your comments, but I'm going to stick to my guns on this one. And if something changes, we can always change it later, but I think I'm going to stay there with a low rating on it.

And there was another one I had, which was tris(1,3-dichloro-2-propyl) phosphate. There was a question that we upgrade that from medium to high.

I looked at this pretty carefully. And, yes, I went through the human use where there is homes, offices, drapery exposure, et cetera. This one had no cancer epidemiology studies at all. It did have very strong animal carcinogenesis studies, which I liked, in a sense that they were done well. And there were renal cortical tumors in males and female and Sprague Dawley rats. There were testicular tumors in males that was dose dependent. Hepatocellular tumors and was dose dependent in females. No genetox data and was not evaluated by IARC or EPA.

So I thought medium was -- I was comfortable with a medium classification for this one. If there's more data or something, then I'm happy to look at it.

But I was comfortable with my decision there. So thank you for your elegant comments, but again I'm going to stick to my guns. I do not feel compelled to move on

this one. And I think that was it for mine, is that right?

CHAIRPERSON MACK: Okay. Anna didn't have any that were commented upon.

COMMITTEE MEMBER LANDOLPH: Permethrin, Tom, there was a comment.

Yeah, and that was mine too.

I have in my notes that there were malignant lung tumors induced in the old early mice studies. I have to go back and look at that again.

And there were -- most of the studies were benign tumors, negative in a number of rat studies, negative in the biomouse study. EPA says likely to be carcinogenic as of 2002. And typical Type I pyrethroid insecticide. So we know a lot about it.

And I think your request was to downgrade this one. And I would say probably the best I could do on this one, I think -- I do agree that most of the studies were benign lung tumors. I was a little bit concerned that benign tumors kept popping up over and over again, and that one mention of malignant lung tumors, which I'll have to go back to check.

I was certainly influenced by the EPA's panel considering it. Likely to be carcinogenic to humans by the oral route. That swayed me a lot.

So I think I'm going to stick to my guns on this one too and thank you for your comments, but I think I'm going to stick with medium on that one too.

CHAIRPERSON MACK: Okay. David.

COMMITTEE MEMBER EASTMOND: Let me just say, I appreciate the public for their comments. And I think they made -- for the two compounds that I'll be commenting on, I think they made some really very valid points.

However, in my mind, you know, this sort of screening level exercise is not possible to get into great detail on the tumors and the types of tumors, and really the relevance of those tumors, because if we do that, we're doing the full assessment. So it's very hard to do that.

My take on this is that while -- and particularly this is with PFOA at this point. You know, there were very good arguments made. And it's likely that in a full screening of this, those arguments will come forward and we would certainly evaluate that, and critically evaluate them. And there's by no means certain that we would even list this. But at a level of screening prioritization, this is a compound that there's considerable concern within the -- among the public. And it's one that there's a lot of interest in.

So for me, that still tends to drive the thing.

There is evidence in animals. The animal data may be shown to be not relevant to humans. But at this point in time, we don't feel like we should be able to make that decision. And we do know that there's considerable concern among the public about this. Early on, we had numerous organizations that tended to be more concerned about -- environmental organizations or consumer organizations, which were very concerned about this compound.

So that in itself would suggest to me that I would probably keep it at the higher priority. But that doesn't mean it will be listed, because I think it just means it ought to be evaluated in a more thorough basis.

With regards to the DINP, this one again the gentleman from ExxonMobil made some very good points. And the woman also from UCSF -- I'm not sure if -- made some good ones.

You know, the fact that it's no longer used in children's toys and that certainly the exposures are lower than once thought. I guess the first thing is, if that, in fact, is true, that would kind of shift my influence or how -- the exposure on that.

But on the other hand, the woman from UCSF mentioned that by looking at other metabolites, there's actually widespread exposure in a sub-population, and

they're not sure how this is occurring. And so it suggests that maybe there is exposure out there and they're -- it just depends on what you're looking at and how you target this.

The fact that EPA revised their concerns in 2005, which was a comment made by the individual from ExxonMobil, is also -- tends to kind of pull it down a little bit in my mind. I don't -- I guess the real thing for me comes down to the children's exposure, and are there sub-populations that are exposed at fairly high levels?

And I don't feel like I know enough to make a really knowledgeable judgment at this point. So I guess my inclination would be to pull it down in that, where I had it before was between high and medium. And it's still in that category.

So I guess that's what my thinking would be. Let me just look at this really quickly.

MR. RAWSON: You didn't mention the -- my name is Bill Rawson and I'm also with ExxonMobil.

You didn't mention the CHAP and I just would appreciate if, in your comments, you would include that. That specifically looked at the cancer issue and children, if you will.

COMMITTEE MEMBER EASTMOND: Yeah, you might

define what CHAP refers to. That would help me as well.

MR. RAWSON: Sorry, last name is R-a-w-s-o-n, William Rawson.

The Consumer Products Safety Commission convened a Chronic Hazard Advisory Panel, and specifically looked at the issue of cancer and exposure to children when DINP was used in toys. That was the activity where a Senior Scientist at OEHHA participated. And they concluded no significant cancer risk to children. And I'm not trying to re-argue the point. I just was hoping that in your response to comments you would include that in your thoughts.

So that specifically looked at that exposure in cancer and children with products that would be put in the mouth, and said no significant risk.

Thank you.

COMMITTEE MEMBER EASTMOND: Yeah. Lauren, do you want to --

DR. ZEISE: Maybe I can speak to that, because I was a scientist that served on the CHAP Committee. And I think one thing that played heavily in the mind of the Committee was the PPAR-alpha mechanism of action. And that was before all of the most recent data have come in, that would be looked at very carefully in a full review of the compound.

As you noted, questions have been raised regarding that mechanism of action for carcinogenesis.

COMMITTEE MEMBER EASTMOND: Just a comment. And I didn't do the most thorough review on this, but you're really looking at essentially liver tumors, which are believed to be associated with this PPAR-alpha mode of action, which is now being questioned.

You're looking at mononuclear cell leukemias, which have a high spontaneous rate. But, again, as I recall, in the EPA evaluation, they said this appears to be independent of that spontaneous rate. They thought there was dose relationships and that they occurred earlier on than the spontaneous.

So they didn't think that explained the mononuclear cell leukemias, and the renal tubular carcinomas in the rats. Again, this may be this basically alpha-2u mechanism. But from my experience, there are like seven or eight criteria that IARC listed in order to categorize something on that.

And although people say that these criteria have been met, I'm not certain they have been met. And that's where I think that the Committee would be wise to go through them, point by point, if we really are going with these mechanisms. That's something that would take a full evaluation to determine.

So my inclination on this really is probably to keep it where it is. Although, I would put it on the lower level of the high priority.

CHAIRPERSON MACK: Are there any now that we haven't addressed?

Has anybody addressed something that we haven't responded to?

Then I guess we're finished with this process.

COMMITTEE MEMBER EASTMOND: Tom. Well, I guess you've done that. But if others heard the same arguments, they could weigh in, if they felt like it, I mean, among the panel members.

CHAIRPERSON MACK: Let's do that.

Okay. Each of us has expressed whether or not we're willing to change. The question is, do any of the other panel members wish to comment on our responses?

COMMITTEE MEMBER HOPP: I agree with the current changes after the public discussion.

I think we should accept them.

CHAIRPERSON MACK: Okay. I guess we've got our prioritization, like it or leave it, like it or not.

We'll do the best we can each time it comes up -- we come up with a given tumor. And now it's going to be a relief to just go back to the usual review of evidence on a specific compound, rather than prioritization.

I thank you very, very much for your courtesy, your thoughtfulness and your helpfulness, because this has not been an easy process.

CHAIRPERSON MACK: All right. We'll resume at 1:30.

(Thereupon a lunch break was taken.)

AFTERNOON SESSION

CHAIRPERSON MACK: All right. Now, that I've arrived, it's time to start. I apologize for being late.

We're going to go into the discussion of marijuana smoke, so where is Martha.

Go for it, Martha.

DR. SANDY: Thank you, Dr. Mack. We're going to -- the staff will present very briefly the high points that were covered in the hazard identification document, which you all have. And first, we'll hear from Dr. Jay Beaumont on particularly the human data. And then we'll hear from Dr. Rajpal Tomar on the animal data and some of the mechanistic data and from Jennifer Hsieh on some of the mechanistic data.

So Dr. Jay Beaumont.

(Thereupon an overhead presentation was Presented as follows.)

DR. BEAUMONT: Thank you, Martha.

Good afternoon.

Go to the next slide.

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DR. BEAUMONT: I'd like to first describe some of the characteristics of marijuana smoke in a basic fashion. First of all, it's the smoke that's created when the flowers, leaves, stems, seeds and/or resins of marijuana

plants are burned. The smoke contains thousands of compounds. Some are in gas phase, some are in particulate phase and some are semi-volatile. The compounds are both -- some are organic and some are inorganic, including metals.

Approximately 350 constituents have been analytically identified. And those are listed in Table 1 of our draft document. And unique to marijuana smoke is that many cannabinoids are present. Over 60 have been identified. The most notorious maybe is Delta 9-THC, because it's the most psychoactive ingredient.

And then 33 of the individual constituents are already listed as Proposition 65 carcinogens. And those are listed in Table 6 of the draft document.

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DR. BEAUMONT: Regarding its occurrence in use. It has been smoked in many parts of the world for thousands of years. However, in the United States in other western cultures, marijuana smoking became popular in the late 1960's and 1970's. And in a moment I'll show you a little more data on that.

In California, since 1996, it has been legal for physician-recommended purposes, because the voters of the State passed Proposition 215, the Compassionate Use Act.

And then one final note about it's use, is that

in many parts of the world, it is mixed with tobacco prior to smoking, especially in North Africa and in Europe. And that has implications for the epidemiology studies that we'll see in a few minutes here.

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DR. BEAUMONT: This slide or graph shows the marijuana first-time use rates per thousand people per year in the United States over the period 1965 to 1998. And the main reason we want to show this slide is to show when it first became popular, which was the late 1960's. Just by chance I saw the film Woodstock last night.

(Laughter.)

DR. BEAUMONT: It was prevalent then.

(Laughter.)

DR. BEAUMONT: In the 1970's it plateaued and since then it's had some ups and downs in popularity. But basically, it has remained popular.

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DR. BEAUMONT: I'll now turn to a discussion of the human epidemiological studies. This slide is labeled "Controlled Cancer Studies". Just to be clear, that we are not including case reports, case series, review articles that sort of thing. These are all controlled epidemiological studies.

And we've identified a total of 26 such studies,

of which 21 reported results for direct marijuana smoking and six reported results for smoking by parents in studies of childhood cancers.

And two things I need to point out. One is for the parental smoking studies, it says six. The draft document says eight. That's because one of the articles pooled data from three studies. And so we initially counted it as three studies, but they didn't report results for the individual studies. So I think it's now more fair to say that was a single study. So a total of six studies.

And then one more thing, you might have noticed that 21 and 6 don't add up to the total 26 up top. That's because one of the studies of childhood cancers reported results for both smoking by the parents and smoking by the children. So that was direct smoking.

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DR. BEAUMONT: There are many epidemiological studies. And they have some validity issues in common. So I thought it might be good to start with a preview of what those validity issues are.

One type of issue is information bias from several sources. One of the most important ones probably is underreporting of marijuana smoking. And this is due to its illegality, social stigma, employment restrictions,

and often lack of privacy during interviews.

And I should say that almost all the studies are case control studies, where oral interviews were the method of collecting the data. And marijuana smoking has been illegal in all the countries where the studies have been done.

If the underreporting is equal in case control studies, if it's equal in the cases and the controls, then actually there's no bias. But if cases, for example, underreport less, then healthy controls -- then that would lead to a bias in the ratio estimates.

Another type of information bias is from the use of proxy interviews. And this comes up in the studies of parental smoking by fathers, where many of the fathers didn't participate and the mothers answered the questions for the fathers. And it's hard to say what direction the bias might go if there was one. Another type of bias is confounding bias from adding tobacco to marijuana. I mentioned that earlier.

Also, many studies had low rates of participation by subjects. And so there was potential for selection bias. And then finally, cancers caused by exposures in the environment usually have a latent period often over 20 years before the carcinogen is expressed. And some of the studies had a relatively short observation period. And

I'll point those out.

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DR. BEAUMONT: This next slide lists all of the cancer categories that have been -- for which results for marijuana smoking directly by humans have been reported. So there's a total of 19 different cancer categories, for which results have been reported. There's one category, head and neck. By the way, these are in alphabetical order. There's overlap with the head and neck cancer category and several other categories. Otherwise, I think there's little overlap.

Let's see. For each cancer category, at the end in parentheses, is the number of studies that were -- they found as significant, statistically significant association over the number of studies that have been done, that reported results.

Let's see. I'd like to point out that for 14 of the 19 categories, only a single study has been published so far. Let's see, for five of the categories, there has been at least one statistically significant association reported. And those are bolded and also the number of studies positive is shown in red. So that studies for which there's been at least one positive report have been bladder, brain, head and neck, lung, and testes.

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DR. BEAUMONT: I forgot to say, I'm now going to talk about just those categories where there was at least one significant association. And I'll do this in the order of the number of studies. So the category that had the most studies was lung cancer.

Oops, I somehow skipped. Let's see if I can go back.

Sorry about that.

Six studies have reported results for marijuana smoking and lung cancer. The first thing I'd like to point out is the last column of example rate ratio estimates -- by the way, some studies are case controlled, some are cohort, but they're all trying to estimate the rate ratio. So even they might have reported an odds ratio, I've listed these all as rate ratio estimates.

The first thing you might notice is that the results disagree from a ratio of as little as 0.6 up to a high of 8.2.

The second thing I'd like to point out is that three of the studies were conducted in northern Africa, where it's common to mix tobacco and marijuana. And this is acknowledged by the authors of those articles. And that's the study in Tunis, one in Casablanca, Morocco. And then a second study in Tunis, but done at a later time period with different subjects.

And because those three northern African studies, I think, are of questionable validity, to be nice, because they mixed tobacco with their marijuana, I personally dismiss them, and I'd like to focus on the other studies, starting with Sidney 1997, was a prospective cohort study in the bay area. It was actually members of the Kaiser Permanente health plan who filled out a questionnaire. And using an exposure classification of seven or more joints ever in their lifetime, they reported results separately for men and women. And they did not find excess risk in either group.

A limitation of this study was it ended cancer observation in 1993, which is approximately 25 years after smoking became popular in the U.S. So it may have been too short to observe cancer if there was a risk.

I'd like to skip down now to the Hashibe 2006 study. This was a registry based case control study in Los Angeles county using population controls. And they found in their highest exposure category of 60 plus joint years -- and I'll stop to explain joint years. One joint year is equivalent to smoking one joint per day, every day for a year. So 60 plus joint years is substantial exposure. And they found a rate ratio estimate of 0.6.

They also nicely looked at a subset of subjects who were not smokers of tobacco. And in that subgroup

they had a smaller number of subjects. And their highest exposure category was one plus joint years, but again they found no excess risk.

Now, skipping down to Aldington, a study in New Zealand, which is another location where like in the U.S. it has not been common to mix tobacco with marijuana. This study found slightly increased overall for ever smoking marijuana. But in their highest exposure category of 10. -- over 10.5 joint years, they did find a significant association of -- a rate ratio of 5.7.

I'd like to point out that in all of these studies, except for the Sidney cohort study, the questionnaires were administered orally, and in particular in the Aldington study in New Zealand, the interviews took place in the subject's homes.

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DR. BEAUMONT: This next slide shows the four studies that have reported results for head and neck cancer. And I'd like to note that the draft document only listed three studies. That's because this Berthiller et al. study was published after our draft document was distributed.

Again, we find a diversity of findings, ratios ranging from .9 up to 6.4. But all of these studies were done in locations where marijuana and tobacco are not

mixed, so that's good. The first study was a case control study in a hospital in New York City by Zhang et al. Using a definition of ever smoking marijuana, they found a rate ratio of 2.6. A validity issue in that study was the use of blood donors at the same hospital as the control group.

And the authors of the study acknowledged that blood donors may use marijuana more or less than the general population.

The next study published was by Aldington again in New Zealand. And this actually came from the same study that reported lung cancer that we saw earlier. And, in fact, it had the same control group. But for head and neck cancer, they did not find a significant association -- I show the results for ever smoking, even in their highest exposure category, they also did not find a significant association.

The next study by Gillison et al. was another registry based case control study in Los Angeles county using population controls. And this was a study that focused on risk factors, in general, for head and neck cancer, and within strata of human papilloma virus negative and human papillomas -- I'm sorry, Type 16 positive. And HPV virus is a known cause of cancer. It is classified by IARC as a carcinogen.

Well, they found among the HPV 16 Negative cases an odds ratio of 2.0 that was not significant. But for those subjects who were HPV 16 positive, that ratio was statistically significant. And the authors speculated there may have been some interaction. They could only guess or speculate about causality between HPV 16 and marijuana smoke.

And then the most recent study by Berthiller combined or pooled data from case control studies in Seattle, Tampa, Los Angeles, Houston, and seven cities in Latin America, mostly in South America. Some were registry based. Some were hospital based. At any rate, overall for ever smoking marijuana, they reported an odds ratio of 0.9, not significant.

Among subjects who hadn't smoked tobacco, interestingly, still an odds ratio of 0.9. And then in a subgroup, even smaller of non-tobacco and non-alcohol, because alcohol is also a risk factor for head and neck cancer, a slightly increased ratio of 1.1 that was not significant.

In their highest exposure category of over five joint years, they did not find overall an elevated odds ratio. I hate to do this, but I'm going to back up to the lung cancer slide for a moment, because -- see the Berthiller -- Berthiller on this head and neck slide, they

also have since published another study on lung cancer. And it was data pooled from three North African studies. They used data -- Sasco 2002 data from Casablanca. They used the Voirin 2006 data from Tunis. And then they had data from a new study in Algeria, also in northern Africa. And I discount this new pooled analysis again, because of the mixing of tobacco and marijuana.

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DR. BEAUMONT: Moving forward this time. This slide shows results for three categories of cancer, because they're smaller numbers of studies. So here we have bladder cancer, brain cancer and testicular cancer. Two studies reported results for bladder cancer. They disagreed with each other. The first study was conducted in Egypt, Northern Africa, but it did not find excess risk.

The second study was conducted at Veteran's Administration Hospitals in Palo Alto and Augusta, Georgia. They did not report adjusted odds ratios. But in a regression analysis, they did adjust for cigarette smoking and other factors. They said the coefficient for marijuana -- cumulative marijuana smoking was statistically significant at the .01 level.

For the single study reporting results for brain cancer, using the same cohort we talked about for lung

cancer, it was the Kaiser Permanente members' cohort in San Francisco and Oakland. For ever one or more times -- smoking marijuana one or more times per month, they did find a significant odds ratio of 2.8.

The one study reporting results for testicular cancer conducted in the Seattle Puget Sound region, this was a registry-based control study. First, I'd like to say they divided the cases into seminoma and non-seminoma and mixed cancers, and reported results separately for those two types of cancer.

Well, among former marijuana smokers who had ever smoked marijuana, they found slightly elevated odds ratios. They were not statistically significant. However, among current marijuana smoking, they found a significant elevated risk, but just in the group of cases that was of non-seminoma and mixed type.

Again, all of these studies used orally administered questionnaires. And so underreporting was an issue.

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DR. BEAUMONT: Okay. That's the end of the discussion of the human studies.

This slide now reports the cancer categories, six of them, that have been reported for smoking by parents and cancers in children. And you'll see that there have

been few studies of each cancer type per category. But almost all of them have had a significant association reported.

Some things that are important to know about these studies is -- one, is that they were all conducted under the auspices of the National Cancer Institute funded Children's Cancer Group. And they were similar in their study designs. They were hospital based but used population controls matched on phone area code. And they all used telephone interviews of the parents.

Well, the next slide shows --

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DR. BEAUMONT: -- the studies that reported results for maternal marijuana smoking, and found a significant association, the first by Robison et al. of acute myeloid leukemia reported a 10-fold odds ratio, but did not give a specific number. But they said that it was significant at .005. And that was for having used marijuana, smoking it five or more times in the year before or during pregnancy.

The study by Bluhm et al. of neuroblastoma did not find a significant risk overall for the 10 months before birth. But in the first trimester, they did find a significant association and odds ratio of 4.8.

And then finally the study rhabdomyosarcoma by

Grufferman et al. reported an increased risk 3.0 odds ratio for ever use in the year before birth, by mothers. Okay, that's for mothers.

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DR. BEAUMONT: The next slide shows results for smoking by fathers. And here we have five categories of cancer, for which a significant association has been reported. And the results -- the odds ratios are pretty similar, ranging from 1.4 to 2.

Let's see, the first row for Wen 2000 reported results for leukemia of all types combined, and reported an odds ratio of 1.5 for children of all ages - I think it was up to age 18 - for smoking ever by the fathers in the year before the birth. They also did a separate analysis for just the infant leukemia's. And that odds ratio was a little higher at 2.0.

And then Wen et al. also reported an analysis for the subgroup of acute lymphoblastic leukemias and using the same exposure definition found an odds ratio that was significant.

And then Trivers et al. in 2006 reported results for acute myelogenous leukemia and found a barely significant odds ratio of 1.4 for ever in smoking by the father, regardless of time period.

Bluhm et al. in 2006 reported results for

neuroblastoma. This is the same Bluhm neuroblastoma study for which results for mothers was reported in the previous slide. And for fathers they reported an odds ratio of 2.0.

And then finally for rhabdomyosarcoma, the same study as in the maternal slide, for fathers they also found a significantly increased odds ratio. Something very important to know about these studies of the father smoking, is all the studies, except for the Bluhm study -- actually, all of the studies had very poor participation by the fathers. And all of the studies, except Bluhm, interviewed the mothers when they couldn't contact the father. And so they had very high numbers of proxy interviews.

The Bluhm study did not use proxy interviews and just had very low participation rates by fathers. So that was a potential selection bias.

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DR. BEAUMONT: I'd now like to turn the microphone over to Dr. Rajpal Tomar.

DR. TOMAR: Thanks, Dr. Beaumont.

I'll describe in detail in the marijuana smoke doccument. There are four carcinogenicity studies exposing animals to the marijuana smoke or marijuana smoke condensate.

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DR. TOMAR: In the marijuana smoking inhalation study groups of 20 female Wistar rats were exposed for 15 minutes per day, six days per week for 36 months. The marijuana smoke was generated by burning 0.6 grams plant material of marijuana.

The author did not give the tumor incidence data. However, they indicated that 50 percent of the animals developed tumors as compared to none in the control. The tumors described were benign serous cytoma of the ovary follicular cysts of the ovary. And benign adenofibroma telangiectatic cysts and polyps and malignant adenosarcoma of the uterus.

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DR. TOMAR: In the marijuana smoking condensate is a group of newborn exposed to concentration of marijuana smoke condensate on Days 1, 4, 7, 11, 14 and 18 of life.

Again, the author did not give the tumor incidence data, but they indicated that only those groups, which received 194 milligrams of condensate developed tumors. The tumors described were mesenchimatous tumors composed of two or more undifferentiated cells invading the dermis and infiltrating the skeletal muscles. These type of tumors usually develop from mesenchymal stem cell

or by the conversion of epithelial cells to mesenchimatous.

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DR. TOMAR: In these two skin-painting studies of carcinogenicity as well as tumor promotional study, the author compared the carcinogenicity of marijuana smoke with the tobacco smoke.

In the carcinogenicity group, groups of 100 Swiss mice were painted with 75 milligrams of tar on the back of the skin three times per week for 74 weeks. The tumor incidence was six out of 99 in the marijuana group as compared to 14 out of 97 in the tobacco group.

While there was no concurrent control in this experiment, the author indicated that in their laboratory they rarely observed tumors in acetone-treated animals. In the case of the tobacco, there were two carcinomas besides the squamous cell papilloma.

The author indicated that in this experiment both marijuana as well as tobacco smoke are considered carcinogens.

In the case of the tumor promotion study, groups of 60 Swiss mice were initiated with 75 micrograms of dimethylbenz[a]-anthracene. After 10 days they were painted with three times per week for 56 weeks with 75 milligrams of the tar. The tumor incidence in case of the

marijuana was 26 out of 60, which included the squamous cell papilloma, carcinomas, as well as three fibrosarcoma. In the case of the tobacco, there was squamous cell papilloma and carcinoma only. There were 34 out of 60, as compared to the initiated group alone, which has five out of 60.

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DR. TOMAR: Given the complexity of the marijuana smoke, it is difficult to determine the precise mechanism by which marijuana smoke induced cancers. However, based on the study of marijuana smoke and what is known about the individual components, the number of possible pathway mechanisms can be envisioned.

Besides the similarity with tobacco and marijuana smoke, as well as the similarity in the biological effect, suggests that these two smoke components probably share the common mechanism.

This figure indicates that five possible mechanisms by which marijuana smoke may induce cancer. Genotoxicity is likely the mechanism of action. As we will show in the next few slides -- as we show in the next few slides, marijuana smoke as well as the individual components have been shown to cause chromosomal abnormality as well as gene mutation.

Immunosuppression is a known cause for increased

spontaneous as well as chemically-induced tumors. Marijuana smoke, as well as Delta 9-THC, which is a major psychoactive component of the marijuana smoke is immunosuppressive.

Many of the studies show the sustained inflammation. Sustained inflammation brings a lot of leukocyte, which release reactive oxygen in species and inflammatory cytokine, which can cause gene mutation. And this is a known cause -- again known cause of the carcinogenesis.

Delta 9-THC and other cannabinoids bind to the CB1 and CB2 receptors -- activating the cancer as well as inhibiting the -- this links to the multiple changes in the pathway, which affect the cell proliferation, differentiation, as well as cell death.

A number of mechanisms are known to affect the hormonal pathway. And these again affect the cell proliferation, as well as the differentiation of the cells, especially in the reproductive organs. In fact, one of our -- the first study indicates all reproductive tumors in the carcinogenicity study.

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DR. TOMAR: Now, I'll talk about unusual Components.

As described before, in human studies, increased

lymphocyte hprt mutations were observed in mothers and who smoked marijuana and their newborns.

There are also studies, which shows the increased DNA and chromosomal damage in peripheral lymphocytes, bone marrow preparation, as well as alveolar macrophages obtained by lung lavage from a marijuana smoker.

In addition, marijuana smoke condensate increased mutations in Salmonella. And a number of individual chemical constituents of marijuana smoke are genotoxic, especially the polycyclic aromatic hydrocarbons, benzo[a]pyrene being a prototype of PAH has been shown to induce p53 suppressor gene mutation. And these mutations are very common in the lung cancer patients.

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DR. TOMAR: Immunosuppression or immunoenhancement, this is a two-edged sword. In case of the suppression, you expect increased infection and increased tumor. In the case of the enhancement, you expect the autoimmunity. Marijuana smoke increased the -- sorry, alveolar and macrophages obtained from marijuana smokers, showed a reduced tumorcidal and bactericidal activity. Similar results were obtained in the animal models, especially in the rats.

There is a study showing the increased progression from HIV infection to AIDS in marijuana

smokers. We know that this increase from HIV to AIDS related to the reduced T cells, again indicating the reduced immunity in the presence of the marijuana smoke.

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DR. TOMAR: Delta 9-THC is a potent immunosuppressive agent. It reduces the thymus and the spleen weight and cellularity. And it does so by binding to the CB2-receptor and inducing apoptosis.

It disrupts the host resistance to microbial infection; macrophage function; natural killer; and T cell cytolytic activity; macrophage and T cell cytokine production.

It needs to be noted that these all effects are observed equally well in CB1 and CB2 mice, that suggest that either there are receptors other than CB1 and CB2 or there are various mechanisms by which the immune system can be suppressed.

We also noted there increased viral hemagglutinin titer and decreased macrophage and T helper cell and CD8 cytotoxic T cell count.

There are varied effects of marijuana smoke or especially the Delta 9-THC on tumor induction. For certain tumor types, there's an increase in the growth of the tumors, especially the lung and the breast tumors. For adults, especially leukemia, there is a decrease. But

this seems to be dependent on what are the mouse models, especially in the wild-type mice, most of the cases there's an increase. However, in case of the nude mice, Delta 9-THC seems to suppress the tumor induction.

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DR. TOMAR: There are inflammatory changes in the lungs of marijuana smokers, inflammation, proliferation and preneoplastic changes have been observed. Similar in animal experimental models, dose-related inflammatory and proliferative lesions. In dogs, bronchiolitis and metaplasia. And in the monkey, inflammatory fibrosis and metaplasia.

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DR. TOMAR: In the mouse skin, there's an increase in sebaceous gland metaplasia. It is similar to the tobacco smoke. And this is a preneoplastic change known to be converted to the tumors in case of the tobacco smoke.

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DR. TOMAR: Now, I'll pass it on to Dr. Hsieh.

DR. HSIEH: Okay. The effects on the endocrine system.

Marijuana smoke and its components can impact endocrine function through multiple pathways. Many of these effects involve the hypothalamic-pituitary-gonadal

or HPG axis, which is shown here.

While other effects are independent of HPG axis, the cannabinoids in marijuana smoke affects the HPG neuroendocrine system, through binding to a cannabinoid receptor Type 1 within the hypothalamus, right here, and binding to cannabinoid receptor Type 2 and the cannabinoid receptor Type 1 within the testes in males, and the ovaries and uterus in females, resulting in alterations in the levels of several different hormones.

Specifically, exposure to the cannabinoid in marijuana smoke has been shown to inhibit the release of gonadotropins, such as right here -- sorry, I couldn't use this pointer -- FSH, LH, prolactin, growth hormone, and the thyroid stimulating hormone and to stimulate the release of the corticotropins, and testosterone in males and estrogen and progesterone in females.

These alterations in endocrine function can have profound effects on metabolism, lactation, and reproductive system function. They can affect the growth of hormone-responsive tissue, thereby increasing the risk of cancer at these sites.

Next slide.

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DR. HSIEH: Okay. This slide shows the various mechanisms by which marijuana smoke and its components

affect endocrine function, both through HPG-dependent and HPG-independent pathways.

First, they are direct estrogen receptor mediated effects. The chemical component within marijuana smoke is able to bind directly to the estrogen receptor to influence uterotropic effects and also stimulate estrogen responsive gene expression.

The indirect estrogen receptor mediated effects.

Chemical components within marijuana smoke, such as PAH, polyaromatic hydrocarbons, is able to interact with the aryl hydrocarbon receptor, and AhR cross-talk with the ER make it plausible right here.

The chemical component within the marijuana smoke will inhibit aromatase further to influence the formation of estrogen levels within the cell.

Cannabinoid receptor mediated effects. As I described in the previous slide within the HPG axis, the cannabinoids can bind to the cannabinoid receptor, further influencing the hormones -- the various hormone secretion within HPG axis. And also cannabinoid receptor can cross-talk with EGF receptor signaling pathways to accelerate cell proliferation

The next one.

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DR. HSIEH: Androgen receptor mediated effects.

The chemical constituent in marijuana smoke inhibit the binding of the dihydrotestosterone to the androgen receptor. And the cannabinoid can affect androgen metabolism in the testes as well.

Next one.

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DR. HSIEH: This slide we are going to discuss the comparison of marijuana smoke and tobacco smoke. Marijuana smoke and tobacco smoke indeed share many similar characteristics, such as:

The first one, the most chemical component that we see in these two smoke are really similar, except marijuana smoke contains cannabinoid and cannabinoid derived product. And tobacco smoke contains only nicotine and the nicotine-derived product.

The next one.

Similar particle size distributions for both marijuana smoke and tobacco smoke.

The next one.

A study report found four times greater marijuana smoke tar is deposited in the smoker's lung than tobacco smoke tar is deposited in the smoker's lung, based on a similar amount of plant material.

The next one.

There are 33 Proposition 65 listed carcinogens

present in both marijuana smoke and tobacco smoke.

The last one.

Both marijuana smoke and tobacco smoke induces similar effects in mouse skin, both with regard to tumor induction, tumor promotion and preneoplastic change. Both induce mutations in Salmonella and both induce inflammatory and preneoplastic changes in the lung of smokers and in the dog lung as well.

The next one I'm going to pass the microphone to Dr. Tomar and he will make the overall summary for today's presentation.

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DR. TOMAR: Thanks, Dr. Hsieh. Just to sum it all up. There is evidence from some epidemiological studies, which suggests that cancer is from direct and parental marijuana smoking.

However, there are some limitations of the epidemiological studies, which include the small number of studies for most cancer types. And in certain studies there is potential biases for mixing tobacco and marijuana; differential underreporting of use between cases and controls; low participation in some; and proxy interviews in others.

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DR. TOMAR: Marijuana smoke or its condensate

induce skin papillomas in mice, and malignant uterine and mesenchimatous tumors as well as benign ovarian tumors in rats. Marijuana smoke condensate exhibits tumor-promoting activity in mouse skin, similar to that of tobacco smoke condensate.

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DR. TOMAR: Studies in smokers suggest that marijuana smoke induces mutations and chromosomal abnormalities. Marijuana smoke condensate induces mutations in Salmonella, similar to tobacco smoke condensate.

Marijuana smoke suppresses the multiple parameters of immune functions.

Marijuana smoke affects multiple hormonal and other cell signaling pathways, leading cells to potential tumor transformation.

Marijuana smokers' lungs exhibit lesions similar to those of the tobacco smokers, including inflammation, proliferation and preneoplastic changes.

Marijuana smoke induces preneoplastic lesions in mouse skin, similar to tobacco smoke.

And then marijuana smoke contains 33 of the same carcinogenic constituents as found in the tobacco smoke.

Thank you very much.

CHAIRPERSON MACK: Thank you, Rajpal.

Now, we'll begin with the Committee's discussion and we'll start with Anna.

COMMITTEE MEMBER WU: Okay.

CHAIRPERSON MACK: Start with a brief pause.

COMMITTEE MEMBER WU: Okay. I guess some of my comments really pertain to the fact that I think the summary from the scientists, I think, you know, describe the limitations of the study.

Maybe before I actually go into the discussion of the studies. I have some problems with the work of the control studies, because I understand that these are observational studies with controls. But I think that the heading is a little bit misleading. And I think that they sort of -- I understand what you're talking about, but I think they're really case-control and cohort studies. And there's really only one cohort study in the document.

But that's just a minor point. But that's just sort of how they're being described.

I think the issues in terms of limitations of the study, because of how issues of underreporting confounding by various lifestyle factors, mostly alcohol. I think one of the things that would be helpful and maybe that will be a way of actually trying to compare the studies, is that within the document you discuss how the different assessments were varied, but -- and I think some of these

questionnaires actually were really limiting to people. They already defined for them, as an example, that exposure means that they have to smoke X amount. And so I think the baseline group and also how they actually -- what is considered exposed would have been very helpful, because I think one of the issues is really how much underreporting -- cases and controls underreporting to this same extent.

So I think if there's a way of summarizing, first of all, what are the questions that were actually used in these -- in these various studies. Second, that they actually have a definition of what is exposed. And then third, what is the baseline group for the comparison, so that you can actually maybe have a better sense of what are the potential under-estimations in terms of exposure.

And I think now that there is really a body of literature in both the adult and childhood cancer, that maybe you can actually see over time, we know what are the cohort changes in terms of prevalence of marijuana use, that you can actually get a sense of whether that's -- you know, whether you can actually have some additional insight to that.

And I think the second question or comment that I have really relates to the issue of what percent of the cases and controls in the various studies were

non-smokers. And I know throughout the document, there was information on that. But I think it will be very helpful, maybe there is an additional table, where you could actually summarize if there were actually data on non-smokers, so that you can actually see among the few studies that actually analyze the data among the non-smokers, what is the evidence.

And I think one of the other points I had was most of the studies actually had information on various levels of exposures. But it was not very clear to me how many people actually analyze the data by "never", "former" or "current" marijuana use. And what is "current"? Is it as up to diagnosis date? I mean, is there some kind of window that they were focusing on?

But I was really quite struck by the newer studies in adult cancers where actually longer periods of exposures are used. That the studies -- there tended to be some additional positive studies. And that in the studies on maternal and paternal use where the window of exposure was really related to use within the year or a different part of the pregnancy. That those studies were fairly consistent, even though, you know, there are well-acknowledged limitations in terms of the methods.

And I think that may, in fact, reflect the fact that for the childhood cancers, it was less relevant

really when those studies were being done, since the exposure period was very critical in terms of this relationship to the childhood cancer.

So I think -- you know, I think there's certainly a body of studies that are accumulating that are suggestive.

CHAIRPERSON MACK: So you're coming down basically on the side of thinking that there is a link between some neoplasia in adults and children and past exposure to marijuana?

COMMITTEE MEMBER WU: Yeah. I mean, I think with the one cohort study that was done from Kaiser, the studies -- there were like four, you know, the cites that were considered, most of them actually were very underpowered. So, you know, because of the fact that there were very few cancers.

So even though it looked like there were many cancers that were negative, it was really based on the analysis from the Kaiser cohort study where the number of cases were fairly limited.

CHAIRPERSON MACK: Marty.

COMMITTEE MEMBER HOPP: Unfortunately, I have a lot to say.

First of all, I think regarding the epidemiology studies. I think the basic problem with all these studies

is that the instrument that's being used to evaluate the exposure of the interviewee is poor. It's a very -- it is not an evidence-based instrument. And, in fact, the only time when you tested this questionnaire against reality in any of these studies was when they tested the questionnaire in the Lozano study, where they looked at the incidence of cannabis in meconium. And they evaluated prenatal exposure by the presence of cannabis in meconium.

And they interviewed the mother for using these instruments for exposure. And then they were able to actually tell by tissue analysis whether or not she was telling the truth.

And the numbers are four to one. There was four times greater exposure in the tissue than the mothers were willing to admit.

So that essentially the instruments that are being used to evaluate exposure don't do what you want it to do. If you ask patients -- if you ask people directly face to face, they're not going to tell you the truth. If you ask them, they may underreport they may overreport, both for themselves and their spouse. And the same thing happens in paper interviews.

This is very unusual for epidemiology studies, because for the vast majority of these instruments they're very reproducible. They're very documentable. When it

comes to marijuana, it's very clear that these instruments are ineffective. And I think that's the -- that affects your control use, because the controls -- when you're going to do a statistical analysis, your controls have to be zero. But if your controls really are not zero, then you're unable to show a significant -- you're unable to show a significant bias. You may have bias there, but it's not shown, because your controls are actually not zero anymore.

So it shows a lot -- throws a lot of this off. That's my first comment.

Now, in order -- I'll shorten up my other comments relative to -- I was asked to talk about genotoxicity and carcinogenicity. And I think it's very important that when you talk about marijuana smoke, to differentiate the plant marijuana from the smoke. And we're really here to discuss marijuana smoke and the carcinogenicity of marijuana smoke. And that's different than the product itself that's being sold as a plant.

The smoke itself contains a huge amount of chemicals through pyrolosis, incomplete combustion, as well as normal plant material, that is not necessarily present in the plant itself.

And essentially what you mentioned is very important. And that is that within the smoke condensate,

there are 33 chemicals that have been identified in the smoke condensate that already are listed under Prop 65 as being known carcinogens to humans.

Thirty-three of these are in common with tobacco smoke. And their concentrations some times are higher and sometimes are lower. However, to me the most important factor here was benzo[a]pyrene; benzo[a]pyrene concentration in marijuana smoke was four times that of tobacco smoke. And we're asked here to determine carcinogenicity for chemicals known to cause cancer in humans. Of all the chemicals studied for lung cancer, this one chemical benzo[a]pyrene is one of the few that have specifically been shown to create the metabolic activation that is distinctive to genotoxicity and to affect the p53 gene as well as other codons.

In an article in Science that I pulled up by Denissenko, which is not on your list here, basically shows that the p53 human tumor suppressor gene in human lung tissue at codons 157, 248 and 273 are the specific spots that benzo[a]pyrene affects. And that the N2 position of guanine is the exact position that benzo[a]pyrene affects the genome to cause cancer. It is the specific carcinogen-based cancer-causing material. And this is four times more common in marijuana smoke than tobacco smoke.

I think all the other issues relative to carcinogenicity are very common that you see amongst every other carcinogen. If you consider a lump of tissue that has 33 carcinogens in them, they're going to have an extensive amount of chromosomal damage, all the toxicity studies are essentially positive.

I think what concerns me most about the immune studies is that of the decrease -- the effect of marijuana smoke on the T cells and B cells and killer cells within the body. Of all the things that you can really hurt someone secondarily is that you can take away someone's own defenses from other cancer-causing agents. And that's what marijuana smoke has specifically been shown to do.

I think that the animal studies on toxicity and painting are essentially similar to that of tobacco smoke. I think it's very difficult to, at this time and age, to be able to feed animals especially large animals, tobacco smoke. Although, there are some studies that they actually fed marijuana smoke through a tracheotomy sites in dogs. And they developed lung changes very consistent with preneoplastic changes.

Essentially, if you looked at our charge, that, being that we need to identify chemicals that are known to cause cancer, when I look at this, in summary, I see 33 chemicals that we already identify as causing cancer. And

some of the most nastiest ones are known to be directly exposed to human cancers to be more consistent in marijuana smoke condensate than tobacco smoke condensate. And so I do strongly believe that tobacco -- this has been very effectively shown to be carcinogenic and to contain carcinogenic compounds known to us.

CHAIRPERSON MACK: Thank you, Marty. Does anybody have any comments on either the epidemiology or the animal studies or the short-term tests?

David.

COMMITTEE MEMBER EASTMOND: Sure. I guess, I would agree if I were saying this is likely to be a carcinogen. There's certainly all sorts of evidence that it's likely to be one.

But what I weigh onto this is, has it been clearly shown? And that's the issue. And if you go down through this, I look at the human epidemiology study, it really boils down largely -- the lung cancer, the one study out of New Zealand, because all the other ones are confounded by tobacco exposure, the other positive ones.

The paternal and maternal exposures for me strike me as really peculiar. All of these have relative risks between one and two, which means they're weak associations. Every single one of them is in that range, which I tend to think indicates recall bias. These are

very different types of cancers. So if they were all leukemias or, you know, myeloid leukemias consistent there. But you didn't see it with the other types of neuroblastoma or something, you might think, okay, there's a pattern here. But since they're all about the same magnitude and they're on all different tumor types, that suggests for me more of a recall bias, that's something consistently -- that it's consistent with. And what you were saying is that you can't really trust these questionnaires very well at all.

So I don't have a real lot of confidence in that. As far as the animal studies, again essentially two of these studies, although they're probably carcinogenic, they didn't have controls, concurrent controls at the same time. So you get this real problem, these are older studies. At the time, they didn't run concurrent controls. These are elevated frequencies, but, you know, when you come down to the definition as shown through scientifically valid testing, according to generally accepted principles. And then it's -- you have real problems there.

Now, the one that did the inhalation, which you would like to turn to, unfortunately gives a very poor description. You can't even tell how many animals got the tumors. It just says 50 percent.

So, again, these are, what I would consider to be, quite weak studies from an experimental design and description. And it's really almost amazing, considering how prevalent this agent is and the usage, that there haven't been any really good animal studies done on this, particularly in light of this real problem with the epidemiological studies.

So I have problems with it. I mean, perfectly logical, I mean, you would expect -- it certainly has carcinogenic agents in it. If I were predicting this would be a carcinogen, I would certainly predict it. But I come back to this idea, has it been clearly shown. And that's where I run into problems according to the scientifically valid testing. So I have some real problems with it.

If I were predicting it or calling it or someone came in for advice, I'd say this thing is going to be carcinogenic for sure. But do we have evidence for it? That's my --

CHAIRPERSON MACK: You mean, you wouldn't use it yourself?

COMMITTEE MEMBER EASTMOND: Yeah, I wouldn't use it.

CHAIRPERSON MACK: Joe.

COMMITTEE MEMBER LANDOLPH: Well, this -- I mean

it's very reminiscent of tobacco smoke, so I'm going to disagree with some of the comments that were just made.

I mean, it causes mutations in Salmonella. It causes mutations in lymphocytes at the hpgrt locus. There was very good data that the State presented already on disruption of the HPG axis, and you see ovarian and uterine tumors. And it's got 33 carcinogens in it. And these are not weak, like the stuff we were talking about this morning. There's 4-aminobiphenyl; arsenic; benzene; benzo[a]pyrene; fluoranthene, three isomers, benzofuran, 1,3-butadiene. There's Chromium VI. There's a dibenz[a,h]anthracene, which is incredibly potent. And then there are dibenzpyrenes, which are orders of magnitude more active than benzpyrene. Then there are metals, you know, chromium. There's nickel.

So there's a whole raft of carcinogens in here. So I'm -- this is bad news. It's as bad as tobacco smoke from its constituents.

And then in addition, you're getting genetox in human tissues, you know, at the HPGRT locus. And I think the epidemiology, yeah, there's conflicts in there and confounders. But the head and neck data look pretty good. Some of the lung data looked pretty good. So I'm fairly convinced. I would certainly have no trouble voting on this as a carcinogen.

I mean, I've been on this Committee many years and we've looked at stuff which was an order of magnitude weaker than this. So I have no trouble with this. I'm going to vote in favor of it without any doubt in my mind.

COMMITTEE MEMBER WU: I want to make a couple additional comments about the quality of the epidemiologic data. And especially in relationship to the assessment of exposure. I think that clearly -- I think if you look at the prevalence of use among the controls in the various studies, and now we're talking about various ages of the adults, because the adult cancers covered various ages.

You go from studies that have about -- one to two percent, up to five percent to the study in Los Angeles where about 50 percent of the controls reported using marijuana.

Very often, and I can't say all the time, but I would say most of the time, when you have such varied differences in terms of usage among controls, it is because of the way the questionnaire is being phrased, right. Now, we can never discount the issue of reporting bias among cases and controls or the direction of the reporting bias.

But if the question is structured in the way that, in fact, the investigator is actually defining for you what they would consider as an exposure, that would

also cause these types of variations. So that if you actually tell the subject that I only considered being exposed -- for example, for cigarette smoking, very often the definition is having smoked one cigarette for at least a year. So for marijuana, if their idea is have they ever used marijuana versus have you ever smoked marijuana at least one per month for a certain period of time, that would definitely give you these very tight -- you know, very varied exposure prevalences.

I'm not saying that these are not flawed instruments. But I think the direction of the bias really cannot be assessed. And I think that was one of the reasons why I really recommended that if we go through the instruments to actually -- and it was actually done in the document, but actually saying what was actually defined by the investigator as being exposed. Because ever exposed really is very misleading, because ever exposed could mean ever exposed meaning having just smoked one versus having exposed, meaning that you smoked at least 30 for over, you know, whatever it is.

So I think that will actually help clarify what it means in terms of these very different prevalences of exposure.

I think the table that will -- or the figure that was presented very clearly showed changes of marijuana

prevalence in the U.S. And there are more detailed data on prevalence of exposure by age. That information can be related to the age cohorts of the people that were covered in these case-control studies, so that you can actually get an estimate of what is the extent of under or overreporting among the control groups.

So that data is actually available, so that you can actually look at -- because in -- the U.S. actually has data by each state since 1960 by age group. The percent that first started using marijuana -- I mean, that they actually started you know, percent of initiation, as well as prevalence of use.

So I think given that data, you can actually have some estimate by geographic area of where the study was actually being conducted, so that you can actually say is, you know, what is the extent of misclassification. And I think looking at that in the controls will actually give you an idea of how flawed these are. So I think the combination of actually knowing what the instrument -- what the investigator actually defined as being smoking marijuana in his or her study, and then actually looking at the data among the controls, I think will give you a better sense of the adult assessment instrument.

Now, in terms of the assessment amount, the mothers about pregnancy and, you know, what the father was

smoking around the partner's pregnancy. Granted that one study from Spain showed that, in fact, there was a four-fold difference between self-reporting and the meconium analysis. The fact is those -- all the studies in children's cancer were actually done using one instrument. You can either say they were all flawed, because most of those studies actually came from the U.S., from whatever the children's group is called.

So I think one of the things that actually would be very helpful is to actually find out what other kinds of medications or recreational drugs were actually asked in those instruments, because there are things that you can sort of say -- they're sort of, what do we call it, dummy exposures, to see whether they were all up or all down or whether they actually coexist with the marijuana exposure, so that things that you really don't expect to be associated, you can actually check it out.

And I think, given that that series of studies were all done within the children's whatever, they had a whole bunch of exposures that were asked. So I think for the purpose of really trying to understand is this very wide range of diseases or cancers that were covered, all showed us 1.5 to two-fold increased risk is all due to recall bias or is it because they are really telling you something?

I don't know what the answer is.

I didn't actually think that every -- first of all, 1.5 is not low. 1.5 is important if it is real. ETS is 1.3, you know. And we take ETS very seriously. So I wouldn't dismiss the 1.5 as being not important.

I think the more important thing is to find out whether, in fact, this 1.5 is really because it is all implicating something that is common. And I think given that that series of studies, you know, were done in sort of a very uniform way, in terms of the children's cancer group, there may be an opportunity to find out what other exposures that you wouldn't expect, and other exposures that you would use with recreational drugs like marijuana, and that might provide some insights.

CHAIRPERSON MACK: Sol.

COMMITTEE MEMBER HAMBURG: Anna, having heard all that, and tried very difficultly to comprehend it, I don't see that the human data is interpretable. We can go back. We can reanalyze it. We can look at it a little bit better, but the epidemiological data, I think, is not helpful, at least for me, in determining whether marijuana smoke is carcinogenic or not.

I think that Joe actually analyzed this very appropriately. There are at least 33 known carcinogens within marijuana smoke. The genetic data is relatively

strong. The mutational data is very strong. And I don't see any problem with listing marijuana as a potential carcinogen.

And I don't think we can use the epidemiological data to either sway us one way or the other, because of the difficulties in interpreting it and understanding exactly what the information says.

CHAIRPERSON MACK: I wasn't actually planning on voting because I was an author of one of the studies.

Yeah, I am on.

I said I wasn't planning on voting, because I was one of the authors of one of the papers that she reviewed. But the fact is that I agree with all of you. I'm sure we all believe that marijuana smoke is a carcinogen. But I agree with both Marty and Joe and Anna, that there are -- it's bound to be a carcinogen because there are 33 carcinogens in it.

But I also have to agree with David that it hasn't been clearly shown. And the epidemiologic data, including the study that I'm an author of, is very difficult to interpret. And I wish that Anna's suggestions had been available to the group before, because I think that would have helped a lot. But I have to say that I can't come down voting for listing right now, because of the fact that it's not clearly shown, even

though I believe it to be true.

So are we coming to a vote now?

DIRECTOR DENTON: Okay.

CHIEF COUNSEL MONAHAN-CUMMINGS: No, you're not. You haven't asked for public comment. I don't know if anybody wants to comment, but you should ask for that.

CHAIRPERSON MACK: Are there any marijuana advocates in the audience?

No. Of course, there may be people who have useful things to say.

Anybody have any comments?

Chicken.

(Laughter.)

CHAIRPERSON MACK: Marty.

COMMITTEE MEMBER HOPP: That's better.

Two other comments with regards to the other discussion. First of all, I think that when we discuss chemicals for people in the State of California, I think that we have to look at when this marijuana smoke is being used, and how that can be interpreted towards safety with the studies that we have.

In other words, it's one thing to discuss marijuana smoke and the exposure of 33 carcinogens to someone like myself who, knock on wood at this moment, is fairly healthy. It's another thing to expose someone who

has no T cells, no B cells, no immune response whatsoever because they're undergoing chemotherapy for breast cancer or ovarian cancer.

These patients have no inborn resistance to anything. And I think that they're asking us and this committee is, are they being exposed to a carcinogen to which they have absolutely no defenses, if they smoke marijuana while they're in this medical condition?

And I think that question is very apropos to the data we have. That's different than the epidemiology data that we have. That's the question that goes back to the carcinogenicity within this chemical. This is not epidemiology. This is carcinogenicity. And to these patients who have absolutely no resistance, I think that the carcinogenicity studies that we show here are very dangerous to these people. And I think it is carcinogenic to these people.

Just a second.

CHAIRPERSON MACK: I think you're right, of course, that if a physician is giving advice to a patient with cancer, who is considering taking medical marijuana, you have every reason to give that advice in the way that you say.

COMMITTEE MEMBER HOPP: No. No. The point I'm getting at is that I think that this is carcinogenic to

those people.

CHAIRPERSON MACK: That's right and that's why you give that advice. But the difficulty is that legally that's not the task we've been given, as I understand it. The task we've been given is deciding whether or not, as scientific experts, we can say that marijuana smoke has clearly been shown to cause cancer.

Now, as far as I'm concerned, the closest way that I can get to that is the animal studies. But you guys have described them and have not lauded them in any great way. And I have difficulty then being able to say that it causes cancer in animals from the way you've described the studies.

And I agree with your criticisms of the epidemiologic studies. And I also agree with Anna, that if we knew exactly what was going on in the controls to be able to evaluate the biases present in the case assessments, it would help, but we don't have that right now.

COMMITTEE MEMBER HOPP: No, but what we do have is we've taken this condensate of a group of chemicals and shown that the individual chemicals within that group are carcinogenic. And it's hard for me to understand how you could say that each individual chemical is carcinogenic, but when you put it together, it's not.

CHAIRPERSON MACK: Well, suppose that they counteract each other.

No, of course, I believe they do. But again, you know, if what you say is true, we shouldn't be given the task of judging marijuana smoke, because it would already have been listed by default, because there are 33 chemicals that are carcinogens within it.

COMMITTEE MEMBER HOPP: Which is my point, I don't know why it hasn't been.

CHAIRPERSON MACK: But we were given the task.

COMMITTEE MEMBER HOPP: Because by default, it should have been.

CHAIRPERSON MACK: I either need some advice from Carol or from somebody down there at that bench.

DR. SANDY: This is Martha Sandy.

I'll just say that under Proposition 65, we can't put marijuana smoke on the list, because it contains 35 other chemicals listed on Prop 65. That's why it's coming to you. You have to -- you're being asked about the mixture marijuana smoke, has it been clearly shown?

CHAIRPERSON MACK: Let me ask you, how did it get to your list?

DR. SANDY: We performed the human data screen under our prioritization process of 2004. And there were human data. We brought it to your committee for

prioritization and you recommended that we prepare a hazard identification document.

CHAIRPERSON MACK: So if you'd had sweet pea smoke, it would have been there too?

(Laughter.)

DR. SANDY: I don't know that we have human data on that.

CHIEF COUNSEL MONAHAN-CUMMINGS: Dr. Mack, I think that -- this is Carol Monahan-Cummings.

I think that you're correct that the charge to the Committee is to -- you are correct, that you have to look at marijuana smoke as a mixture or a compound, however you look at it, is it -- has it been clearly shown by scientifically-valid testing to cause cancer?

But I don't think you can exclude your knowledge of the fact that these other constituents of that compound have been shown to cause cancer. I don't think you want to separate those two things from each other, because you're talking about the compound. So I think you might be restricting yourself more than you need to, in terms of looking at it. If you were looking at one of the individual chemicals, then you would want to look at one of the individual chemicals, but you're actually looking at the smoke as a compound.

And so I don't know why you would exclude your

knowledge of the other parts of that compound. We're not asking you to find that any particular part of that is causing cancer. We're asking it as a whole, do you believe it causes cancer?

CHAIRPERSON MACK: So your boss would be quite happy if I simply changed the word to it can be clearly "presumed".

CHIEF COUNSEL MONAHAN-CUMMINGS: No, I'm not saying "presumed". And I'm not speaking for the administration. I'm just saying in terms of consideration of a mixture like this, I don't think that you have to say that the mixture itself has been tested. And I can only look at that data. If it's a mixture that contains a number of other compounds that you've already listed and you know are carcinogens then you can take that into account.

CHAIRPERSON MACK: This is very difficult, because I can't imagine circumstances where a mixture would not have the cumulative effect of its components. That there easily can be things which counteract each other in a mixture. I have no reason in the world to think any of these would do that. So it becomes difficult. And if I were to say -- myself, if I were to say that it has been clearly shown, I can't.

CHIEF COUNSEL MONAHAN-CUMMINGS: And that's

certainly appropriate. That's your scientific judgment based on that information.

CHAIRPERSON MACK: We need to make that decision. And so I think we might as well go to a vote.

COMMITTEE MEMBER LANDOLPH: Yeah, one comment before we vote.

I think in this it's important to realize some historical lessons. And the historical lesson I would point out is that there are very eerie parallels between cigarette smoking and marijuana smoking. As Anna already pointed and I helped review the ETS document of the State, those numbers are small, but they're similar. They have 33 of the same notorious carcinogens in them.

When people first started working with tobacco smoke, it was difficult to induce tumors in animals. They tried by inhalation. It didn't work. So they extracted it. They painted it on the skin and it did work, like it did work here.

And the epidemiology data has flaws in it, granted. But there's a lot of increased incidences at many different organ sites. And the latest Surgeon General's report on tobacco, about a year ago, indicates it effects eight or nine different organs. So I see a lot of parallels between the two.

CHAIRPERSON MACK: Well, I think what you said a

minute ago is the more compelling thing. You said, it did work when you put it on the skin of the mouse.

COMMITTEE MEMBER LANDOLPH: Yeah, and so does marijuana smoke.

CHAIRPERSON MACK: I'm asking about marijuana smoke, not tobacco smoke. I'm saying how good is the data that says it does work producing carcinomas when placed on the skin of a mouse, and under what circumstance?

COMMITTEE MEMBER LANDOLPH: Well, that animal study was a positive study, looking at painting it on the backs of mouse and getting skin tumors, so that was positive. It's good enough.

CHAIRPERSON MACK: Well, that's the basis on which I would decide positively then, because if it causes cancer in the mouse, it causes cancer.

COMMITTEE MEMBER LANDOLPH: Yeah, and of course, you know the skin tumor story is complicated, because first you get papillomas, and a certain fraction, about eight percent, convert into carcinomas.

CHAIRPERSON MACK: But again, it depends on whether it was controlled. In other words, whether there was -- everything was done to the skin of the control mouse except for marijuana smoke.

COMMITTEE MEMBER LANDOLPH: Yeah, I wasn't the primary reviewer, so I didn't pull that original study.

Better ask the primary reviewer that question.

CHAIRPERSON MACK: What do you think of that, Marty?

COMMITTEE MEMBER HOPP: The controls on that were extensive as I recall, because they were the ones who had basic acetone, and all source of solvents, all the different parts, except for the condensate tested that were all negative. And so there were a whole bunch of several controls to try to eliminate every single part of the solvent, compound, irritant and everything else that might have been focused on.

CHAIRPERSON MACK: Okay, if true, that's good enough for me.

DR. SANDY: If I could clarify, though.

CHAIRPERSON MACK: Please.

DR. SANDY: If you're speaking about the Hoffman et al. study, for the bioassay, they did not have concurrent controls. They reported historical controls that had been exposed to the vehicle, which is acetone. And they said the skin tumors in historical controls were very rare. They used the term "very rare", which is usually implying less than one percent incidence. They did have -- in that same paper, they were reported that skin initiation promotion study, where they did have an initiator control group. And you see that both the

tobacco smoke condensate and the marijuana smoke condensate, when applied after the initiator as a promoter, did increase skin tumors. And you had an initiator alone control group there.

CHAIRPERSON MACK: All right. I think we should go to a vote, and we'll see what happens.

Has marijuana smoke been clearly shown, through scientifically-valid testing, according to generally accepted principles to cause cancer?

Everybody answering yes to that question, raise their hand?

(Hands raised.)

CHAIRPERSON MACK: All right. I bought it.

I record five yeses.

And everyone who says no raise there hand?

(Hand raised.)

CHAIRPERSON MACK: One no.

That means that marijuana smoke will be listed.

I feel like a turncoat.

(Laughter.)

CHAIRPERSON MACK: Ms. Oshita.

MS. OSHITA: Good afternoon. As you're aware, your committee last met November 2008. And in a break from tradition, we've called you all back here in just a short six months. And in that time, there still remain

two chemicals that we mentioned at the last meeting. They are for 4-methylimidazole and methanol, which are under consideration for administrative listing. Each chemical has now progressed to the Notice of Intent to the List Phase. And the public comment period for 4-methylimidazole will close today May 29th. We have received comments on methanol already and they will be reviewed.

In addition, in December of 2008, OEHHA announced the possible listing of four other chemicals and they include carbaryl, metam potassium, metofluthrin, and spirodiclofen as chemicals known to the State to cause cancer. There were comments received on each of those chemicals and those are under review as well.

And then lastly, since November, no significant risk levels have been adopted for ethylbenzene. They were 54 micrograms per day via inhalation, and 41 micrograms per day via oral route. And these levels became effective May 7th, 2009.

Thank you.

CHAIRPERSON MACK: Thank you, Cindy.

Is there any other business?

George.

DR. ALEXEEFF: George Alexeeff here. First, I just want to thank the panel members for today's work.

But I just did want to give you a little information about the screening.

So today's screening of 38 chemicals represented our screening of half of the database. So we're hoping in November or December -- well, we're shooting for November, to provide you the rest of the screened chemicals. That's our current plan.

CHIEF COUNSEL MONAHAN-CUMMINGS: This is Carol Monahan-Cummings. I just want to give you a quick update on litigation related to Prop 65. I'm sure you're very aware of some of it. But in terms of cases that went to the court of appeal, we had a decision from the court in the Exxon versus Denton case that you may recall. It had to do with the listing of DIDP as a reproductive toxicant.

The trial court had ruled that we properly listed that under the authoritative body listing mechanism. And the court of appeal agreed and so the chemical remains listed.

The other litigation that's currently pending in the trial court is the Sierra Club versus Schwarzenegger case, which you're all parties to. And that case is currently in the discovery phase. There has been a document production request, as you know. And we've also had one deposition that was started. There's a couple more in the works. And there's a motion next month on the

11th for a protective order for some of the information that's being requested by the Sierra Club.

Some related litigation that I don't think that you knew about or was filed very late in the year last year, was filed by the Chamber of Commerce against the Governor and others. And that case was filed in San Diego county, but was transferred to Alameda county and consolidated with the Sierra Club case.

And that case is only focused on the Labor Code listing process, which you all are not apart of. But there is a provision in the law that requires OEHHA to list chemicals that are identified by reference to certain Labor Code provisions, which also reference some federal regulations under the Federal Hazard Communications Standard.

That litigation, even though it's consolidated, is proceeding much quicker than the Sierra Club case. And we recently had rulings in that case on April the 16th and just this last Wednesday on the 27th. And in both of those, OEHHA and the Administration were successful in arguing that we do have an ongoing duty to list those chemicals, in terms of our interpretation of which lists we need to refer to.

We do expect the Chamber of Commerce to appeal those cases. They've indicated they most likely will --

or those decisions. And so that part of the case will go up on appeal. And the Sierra Club case will continue, but not on those two questions.

Does anybody have questions on these?

COMMITTEE MEMBER EASTMOND: I have a question. It's more general. But during the time we serve on this Committee, we're actually appointed as State employees. And I thought one of the reasons for that was so that we would not -- we could not be sued individually, and yet in this one case that's going forward, we are listed. Now, can you explain what the situation is or what's going on.

CHIEF COUNSEL MONAHAN-CUMMINGS: Yes. You are actually being sued as members of the Committee in your official capacity as members of the Committee, so you're not individually being sued in the same way. You're not going to be personally liable for anything that is decided by the court. But you are being sued as members of this State committee.

And so I would anticipate, at most, that would mean that the court could order you to take some action or not take some action that the Sierra Club is requesting.

COMMITTEE MEMBER LANDOLPH: Yes. That case against the Governor and OEHHA and the CIC involve PFOA and PFOS, I believe.

CHIEF COUNSEL MONAHAN-CUMMINGS: Yes, it does.

COMMITTEE MEMBER LANDOLPH: So should we keep the current PFOA data from the prioritization in our files or should we forward that to you or what do you want to do about that?

CHIEF COUNSEL MONAHAN-CUMMINGS: Well, I don't necessarily want to put attorney-client advice on the record, so I'll speak with you after that.

(Laughter.)

COMMITTEE MEMBER LANDOLPH: Good enough.

DIRECTOR DENTON: Okay. I'll give a quick summary of today's actions of the Committee.

Regarding the prioritization of the 38 chemicals which we brought to you today, you gave us the following advice: Nine of these chemicals were put in the high-priority category, with the one caveat, depending upon the exposure considerations for DINP, put it towards the bottom.

Thirteen chemicals were put in the medium category. Aspartame, it was recommended that that go at the bottom of the medium priority range. And then 16 -- the remaining 16 chemicals were put in the low priority with no chemicals being in the no priority.

And then just a few minutes ago, the Committee voted five to one to list marijuana smoke as a chemical known to the State to cause cancer.

So those are the activities that the Committee undertook today.

I would personally, as one of the individuals who's named on these lawsuits, I would personally like to thank the Committee today for their work. It's always an honor to be part of this work. And you always do the Governor and the State really proud with the work and the consideration that you give these issues that we bring before you.

And I'd also like to give a special thanks to OEHHA staff, to George, to Lauren, to Martha, to Jay, Jennifer, Rajpal, to all of the group that's sitting in the audience who have done such a great amount of preparation for this committee, and I think allowed it to go as smoothly as it did. So I'd like to really extend my thanks as well to Carol and George.

So with that, I don't know if any of the Committee had any other comments or I'll turn it back to you, Tom.

CHAIRPERSON MACK: I just want to second that, especially thank Martha and the group for responding to requests at the last minute. It was very helpful.

COMMITTEE MEMBER HOPP: I'd also like to second that. Martha has been very helpful and the rest of the staff has been very helpful in getting these articles and

organizing this. And I appreciate it.

COMMITTEE MEMBER EASTMOND: I'd like to thank whoever is using the photocopier, because they really got a workout.

CHAIRPERSON MACK: Nobody can say we're all in the same boat, all in the same -- we're not coming from the same place. We're all from different places.

DIRECTOR DENTON: I think we also have to thank Cindy Oshita and Sue Luong who spent many hours doing just that. And to the members of the audience who participated again too.

I guess with that, we're adjourned. So thank you very much.

(Thereupon the Carcinogen Identification Committee adjourned at 3:31 p.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, Carcinogen 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 11th day of June, 2009.

JAMES F. PETERS, CSR, RPR
Certified Shorthand Reporter
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