PUBLIC MEETING

STATE OF CALIFORNIA

ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

PROPOSITION 65

CARCINOGEN IDENTIFICATION COMMITTEE

JOE SERNA JR.

CAL/EPA HEADQUARTERS BUILDING

1001 I Street

SIERRA HEARING ROOM

SACRAMENTO, CALIFORNIA

TUESDAY, NOVEMBER 15, 2016

10:00 a.m.

JESSICA SOTELO
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A P P E A R A N C E S

COMMITTEE MEMBERS:

Thomas M. Mack, M.D., M.P.H., Chairperson

Jason Bush, Ph.D.

Shanaz Dairkee, Ph.D.

David A. Eastmond, Ph.D.

Joseph Landolph, Ph.D.

Peggy Reynolds, Ph.D.

STAFF:

Dr. Lauren Zeise, Acting Director

Ms. Carol Monahan Cummings, Chief Counsel

Dr. Martha Sandy, Chief, Reproductive and Cancer Hazard Assessment Branch

Dr. Amy Dunn, Research Scientist, Reproductive and Cancer Hazard Assessment Branch

Dr. Jennifer Hsieh, Staff Toxicologist, Reproductive and Cancer Hazard Assessment Branch

Michelle Ramirez, Environmental Scientist, Proposition 65 Implementation

A P P E A R A N C E S C O N T I N U E D

ALSO PRESENT:

Richard Adamson, American Beverage Association

Tim Formella, FMC Corporation

Anthony Kriech, Heritage Research Group, Asphalt Roofing Environmental Council

Stan Landfair, Dentons, Sumitomo Corporation, Bayer Agri Science

Arthur Lawyer, Technology Sciences Group, Sumitomo Corporation, Bayer Crop Protection

Lisa Lefferts, Center for Science in the Public Interest

Zhiuei Liu, FMC Corporation

Howard Marks, National Asphalt Pavement Association

Dr. Betti Martini, Mission Possible World Health Inc.

Jay Murray, Murray Association, Calorie Control Council

Gary Roberts, Dentons

Dr. John Ross, Consumer Specialty Products Association

Russell Snyder, California Asphalt Pavement Association

Paul Sohi, Asphalt Institute

Rudolph Valentine, Vinyl Acetate Council

INDEX

P R O C E E D I N G S

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ACTING DIRECTOR ZEISE: Good morning, everyone. I'd like to welcome you to this meeting of the Proposition 65 Carcinogen Identification Committee. We have a -- my name is Lauren Zeise. I'm acting director for the Office of Environmental Health Hazard Assessment.

Today we have one major agenda item being covered, and that is whether or not nitrite in combination with amines or amides should be known to the State to cause cancer. We have some additional agenda items. One covering prioritization of chemicals. Another looking at the degree to which chemicals have been adequately tested for section -- our Section 2700. And we also have some staff updates.

So before getting started, I'd like to cover some housekeeping and logistics. The meeting is being transcribed, so everyone please speak into the microphones. The restrooms and drinking fountains, if you go out the door and turn down -- go out the door and walk down the hall to your left, you'll find the restrooms and the drinking fountains. And then in the event of an emergency, if you follow the exit door, walk down the steps, go out of the building, and convene in

the park across the street. We'll be taking breaks during the meeting for our court reporter.

And now, with that, I'll introduce the Committee, the CIC. So to my direct right is Dr. Thomas Mack from the University of California School of Medicine. To his right is Dr. David Eastmond from the University of California, Davis. Welcome. And Dr. Jason Bush -- pardon --

COMMITTEE MEMBER EASTMOND: California of Riverside -- Riverside.

ACTING DIRECTOR ZEISE: Oh, I'm sorry. Riverside. I've really committed --

COMMITTEE MEMBER EASTMOND: I wasn't offended.

ACTING DIRECTOR ZEISE: My sincere apologies.

To his right Dr. Jason Bush, California State University, Fresno. To my left, Dr. Shanaz Dairkee, California Pacific Medical Center. Then Dr. Joseph Landolph, University of Southern California; and Dr. Peggy Reynolds of -- from the Cancer Institute of California and consulting professor at Stanford University School of Medicine.

And so now I'd like to introduce the OEHHA staff. Carol Monahan, chief counsel, sitting in front. Next to her is Allan Hirsch, chief deputy director. Next to her is Dr. Martha Sandy, branch chief for the

Reproductive and Cancer Hazard Assessment Branch. Next to her is Dr. Jennifer Hsieh, staff toxicologist with RCHAB. Next to her, Amy Dunn, research scientist with RCHAB.

And then for our Proposition 65 implementation staff, we've got Esther Barajas-Ochoa, Michelle Ramirez, and Julian Leichty.

So welcome everyone.

Now, I'd like Carol Monahan to make some -- Monahan Cummings to make some introductory remarks.

CHIEF COUNSEL MONAHAN CUMMINGS: Good morning. I just want to remind the Committee of a few items. I know you've heard this before, but since we only meet once a year or so, I try and do these reminders for each meeting. First, I'd like to remind you that in your binder, and in materials that we've provided to you earlier, there's criteria that was developed by an earlier iteration of this committee for listing chemicals under Prop 65. And so if you have questions about the data that you are looking at for the chemicals in front of you today, please refer to the criteria which are in the back of the binder that you were given today under the tab criteria. Those are scientific criteria that were developed by this committee and early iteration, and the intent of those is to provide

guidance. There's a lot of room for judge -- for scientific judgment calls in the criteria, and that's for a good reason. Obviously, if science moves forward, an application of the criteria has to move with the science. So hopefully that criteria is useful to you in your decision-making today.

The charge for this committee has to do with listing chemicals under Proposition 65. Sometimes, through some of the comments that you hear, you'll be told other information that has to do with the impact of a particular listing; for example, whether or not a warning may be required, what the particular impact on certain sectors of the economy would be for particular listings. While this information is helpful in the general sense, it's not part of the criteria for use by this committee, and so you should apply the scientific criteria that you have available in your binder and apply your own scientific judgment on the questions that are presented to you today.

You'll also hear about the clearly shown standard, which is part of the statute. You are required to find whether or not a chemical or chemical group has been clearly shown through scientifically valid testing, according to generally accepted principles, to cause cancer. This is a scientific

question and is not a legal standard of proof.

This committee is also allowed and often does make decisions based entirely on animal evidence. The chemicals that you are considering today need not have been shown to be human carcinogens, and you don't need to have information about whether or not human exposures to this chemical group are sufficiently high to cause cancer in order to list the chemical group.

The members of this committee are very well qualified scientists. You were appointed to the Committee by the governor because of your scientific expertise, and you don't need to feel compelled to go outside that charge and make other kinds of decisions. In the event that you have or feel you need additional info -- I'm sorry.

In the event that you feel that you have insufficient information or you need more time to think or discuss the question before you, there's no requirement that you make a decision today on any of the questions that will be presented. You can always ask the staff to prepare additional information, or you can ask to defer the question to another meeting.

So today, the Committee is going to be considering whether or not nitrite, in combination with amines or amides, has been clearly shown through

scientifically valid testing, according to generally accepted principles to cause cancer. In this context, the -- this group of chemicals was sent to you because it did not meet the criteria for listing under the authoritative bodies process, and so these don't -- these kind of situations don't come to you very often. Usually we resolve those issues in the administrative process, but this particular set of chemicals has been referred to you for de novo review.

So the Committee today could find that nitrite in combination with amines or amides has been clearly shown to cause cancer; the Committee could find that nitrites in combination with amines or amides have not been clearly shown to cause cancer; or the Committee could defer its decision on this question and request additional information from OEHHA.

In addition to deliberating on the broad group of chemicals encompassed by this term "nitrite in combination with amines or amides," the Committee may discuss potential consideration of one or more smaller groups of chemicals, which are subsets of the broader group; or the Committee could consider other subsets of -- I'm sorry. I already said that.

In the event the Committee identifies the subset of the broader category for consideration, the subset

would be referred for future consideration at a separate meeting so that the public would have sufficient opportunity to comment on the proposed listing. So this is a little bit different than our normal process, so what we are saying today is you can find that the whole group meets the criteria for listing, the whole group doesn't meet the criteria for listing, you need more time to think about it, or you want to consider a subgroup of these chemicals at a future meeting.

Any questions on that? Yes, Dr. Landolph.

COMMITTEE MEMBER LANDOLPH: Can you tell me who --

CHIEF COUNSEL MONAHAN CUMMINGS: Microphone.

COMMITTEE MEMBER LANDOLPH: -- which authorities bodies have --

CHIEF COUNSEL MONAHAN CUMMINGS: The authoritative body that we reviewed, the report was the International Agency for Research on Cancer, and you have that document in your materials. Any other questions? Thank you.

ACTING DIRECTOR ZEISE: Okay. And with that, I'll turn the meeting over to Chairman Mack.

CHAIRPERSON MACK: Thank you, Lauren. In the beginning, the only remark I have to make is I apologize to some extent for asking you to limit yourselves to

five minutes in the discussion from the regulated community. Yes, we might have more time, but part of the reason for the five-minute limit is because, with the exception of the one person or two persons who might be interested in speaking about nitrates, and we can consider an extension for those if it was absolutely necessary, but in relation to the prioritization, because the prioritization is based on information that is self-evident to some extent, the prevalence of the composure, the presence of concern, and the -- and the number of items of information that are pertinent, it really doesn't help us a lot to spend a lot of time on the quality of the information. And because we are not dealing with the details of the quality of the information, public comments are not -- not that useful. They are useful for recording opinion, and we accept the opinion, but that can be done relatively rapidly. So, for what it's worth, I made the decision that I only wanted five minutes from each person.

So with that having been said, I think we'll go ahead and turn it over to Martha.

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DR. SANDY: Thank you, Dr. Mack. I'll say a few words of introduction for why this chemical nitrite, in combination with amines and amides, is before your

committee today, before I turn it over to staff to make the presentation.

So as Carol said, back in February of 2014 OEHHA issued a notice of intent to list nitrite in combination with amines or amides as causing cancer based on conclusions by an authoritative body, in this case, the International Agency for Research on Cancer, or IARC. IARC's conclusions regarding the evidence of carcinogenicity in experimental animals was the trigger for this proposed authoritative body listing. Specifically, IARC included there is sufficient evidence in experimental animals for the carcinogenicity of nitrite in combination with amines or amides.

After considering public comments received on the proposed authoritative bodies listing, OEHHA determined that the scope of what would be covered under the listing of nitrite in combination with amines and amides was broad and covered many more chemicals than had been tested in the experimental animals studies discussed in the IARC monograph. OEHHA found that the proposed listing did not meet OEHHA's regulatory criteria of sufficiency of evidence.

In May 2015, OEHHA announced that nitrite in combination with amines or amides did not meet the criteria for listing under the authoritative bodies

mechanism, and consequently was being referred to you, the CIC, for listing consultation as required by our regulations.

So now let me say a few words about the scope of what is covered by nitrite in combination with amines and amides. Nitrite is common in the environment. It is present in water, soil, and living organisms. It is also common in the diet since it is present at low levels in vegetables, grains, and fish, and it is commonly added to processed meats and fish. Nitrite is also used for various industrial purposes. There are thousands of amines and amides. These are large classes of chemicals that include all amino acids and proteins. As, you know, amines and amides are found in nearly all plant- and animal-based foods.

Some amines and amides are used as pesticides, pharmaceuticals, and industrial chemicals. The materials provided to the Committee to assist in its deliberations include the following: The Committee has Hazard Identification Document prepared by OEHHA. This document includes as an attachment the 2010 IARC monograph on ingested nitrate and nitrite. In the process of preparing the Hazard Identification Document, OEHHA performed focus literature searches to identify relevant studies published since the IARC review, and we

have including the findings from these studies in the documents.

Specifically, our focused literature searches identified epidemiology studies published since the IARC review that assessed nitrite exposure and cancer risk. And just to be clear, none of these cancer epidemiology studies had, as the exposure metrics, nitrite in combination with amines or amides. What they assessed was exposure to nitrite, mostly as it occurs in the diet. Our focus literature searches also identified animal recommended cancer bioassays and genotoxicity studies of nitrite in combination with amines or amides.

The Committee has copies of all the references cited in the Hazard Identification Document and all the relevant papers cited in the 2010 IARC monograph. The Committee has also been provided with the public comments submitted on the Hazard Identification Document.

So now I'd like to turn it over to Dr. Jennifer Hsieh and Amy Dunn, and they'll be making the staff presentations on this.

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DR. HSIEH: Thank you, Dr. Sandy. My name is Jennifer Hsieh, and today we are here to present evidence on the carcinogenicity of nitrite in

combination with amine or amides. This presentation will be a brief summary of the information contained in the Hazard Identification Document prepared by OEHHA. In the attachment to that document, including 2010 IARC monograph, ingest nitrate and nitrite. These materials summarize the finding from a large number of epidemiology and toxicology study. Here is the overview of today's presentation.

I will start with chemical identity of nitrate -- nitrites, amine, and amide, followed by their occurrence and use. My colleague Amy Dunn will then discuss the evidence from studies in humans. I will then continue with the evidence from studies in animals, followed by the mechanistic evidence and other relevant data, mainly focusing on genotoxicity studies.

Chemical identity of nitrite. The structure of the nitrite is shown here. It's a negatively charged ion. Nitrite can form salt with positive charged ions such as sodium and potassium.

Next group amine. Amine are organic compound that contain a basic nitrogen atom with a long electron pair, as shown in red circle here. There are five sub types of amines, included in our review. Depending on the degree of color substitution on the nitrogen atoms, amine can be classified as primary, secondary, linear,

or cyclic; or tertiary, linear, or cyclic. Additionally, partially charge quaternary amine can be formed by sharing a long electron pair with either an archaeal group or aerial group.

The fifth subtype. Cyclic aromatic amine consist of amines where the nitrogen atom is contained within an aromatic agreement.

Next group, amides. Amides are organic compound have a nitrogen atom, which is directly attached to a carbonyl group, as shown in red circle here. There are seven subtypes of amides include in our review. Like amine, amide can be classified as primary, secondary, linear, or cyclic; or tertiary, linear, or cyclic, depending on the degree of a carbon substitution on the nitrogen. Other subtypes of amides including urea, carbamates, sulfonamides, and guanidine.

So continue on the occurrence and use of nitrite. Nitrite is part of a nitrogen circle, and it's common in environment. It is present in water, soil, and organism, such as plant, fish, and animal. In human, in other living things, there is a dynamic interchange of a nitrite and nitrate. Industrial use of nitrite include nitrous acid production, chemical synthesis, inhibition of polymerization reaction, and removal of hydrogen sulfide from natural gas.

Nitrite is present in some foods. Vegetable, grain, and fish all contain very low level of nitrite. In addition, nitrite and nitroso are used as food preservative to cure meat and fish to inhibit the growth of bacteria and to preserve color of the meat.

Next group, amines. Amines are -- yeah, amines are a broad group of chemicals. Amines occur in all leading organisms as amino acid and as biogenic amines, example of which are listed here. Amine tested in combination with nitrite in toxicology study include amine that occur as food constituents, such as meat, fish, milk, and pepper. Heterocyclic amine formed during high temp of cooking. Amine present in tobacco smoke, and amine including cyclic aromatic amine used in rubber, dye, and nylon production. And amine used as coloring or filling agents, as pesticides, and as pharmaceuticals. Several metabolite are amine, and there are various other industrial use of amine.

Next group, amides. Amides are also a broad group of chemical. Amides occur in all living organism as protein and peptides, for example. Amides tested in combination with nitrite in toxicology studies include amides that occurred as food constituents, including meat, fish, milk. Amide formed during high-temperature cooking such as acrylamide. Amides form endogenously

such as methylguanidine. And amide used as pharmaceuticals, pesticides, research chemical, and in synthetic fiber production.

As Dr. Sandy mentioned in the opening remark, overall, amine and amides are large class of chemicals with solvents of individual a member in each class. Both amines and amides are present in plants and animal-based food.

Next group -- next. Nitrites occur in combination with amines or amides in some occupational setting such as those associated with azo dye production; in food, such as plant-based foods and processed meats and fish; and in tobacco and tobacco products.

As discussed in 2010 IARC monograph, ingested just nitrate and nitrite. It has long been recognized that nitrate, when present in combination with amines or amide under acidic conditions, may form carcinogenic and nitroso compound.

Now, I'm going to hand to my colleague Amy Dunn, and she will present evidence from studies in humans.

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MS. DUNN: Good morning. As Jennifer mentioned, I'll be presenting the evidence from studies in humans. Evidence of cars -- sorry.

Evidence of carcinogenicity comes from three main sources: The review by IARC's 2006 working group, published in 2010, that considered 73 cancer epidemiology studies of ingested nitrite. There are also other reviews of relevant studies. The third source is our review of an additional 35 studies, a parallel set to those that IARC reviewed, and these are studies published since IARC's review.

The majority of studies evaluated human exposure to nitrite using estimates of exposure through the diet with the use of food frequency questionnaires. Nitrite occurs in combination with amines and amides in our diet, as Dr. Hsieh has mentioned. Exposure assessment in these studies involved estimating the level of nitrite in foods that people reporting eating, generally using values from the literature, while some studies did measure nitrite in foods. Some investigators only report the combined estimated intake of nitrite plus nitrate.

There are sources of uncertainty with respect to nitrite intake evaluated using food frequency questionnaires. People's diets vary over time. Also, the ability to recall diet is variable. How many of us can reliably say how much of any particular food product we ate last year? In addition, levels of nitrite in

food have been changing over time, and only a few studies took this into account. However, these issues would not be expected to differ by outcome. The uncertainty in the exposure assessment makes it more difficult to find an association should one exist.

A strength of many of the dietary studies is that they took actions to validate the information reported on food frequency questionnaires using follow-up dietary reports or 24-hour diet diaries, among other approaches. An important distinction between case-control and cohort studies is that participants in the cohort studies reported intake prior to cancer diagnosis, avoiding the potential for recall bias.

As I've mentioned -- sorry. The study -- sorry. That wasn't supposed to change.

As I've mentioned, the studies we reviewed were published since IARC's review, and like IARC, were studies that estimated exposure to nitrite. In addition to the dietary studies, one study measured urinary nitrite on a one-time basis and used this to categorize participants' nitrite level. In addition, there were two studies that examined exposure to nitrite in an occupational setting, one in China and the other in Germany.

For studies of nitrite exposure published since

IARC's -- oh, sorry.

There are a number of endpoints of interest in the human studies, and I will go through the evidence of these one by one.

First we will consider the evidence for colorectal cancer. In IARC's review, published in 2010, they looked at one case control study on colorectal cancer, which report an increase risk of colon cancer and an increased risk of rectal cancer. They also looked at one cohort study which saw no association with colorectal endpoints. IARC's review did not consider studies that looked only at processed meat without estimating nitrite content because, as they noted, studies that only evaluated consumption of cured meat and risk for cancer were not reviewed, specifically since they do not represent complete dietary nitrite intake. This is because many, but not all, cured meats contain nitrite, and because other foods can also be an important source of nitrite.

Last year, an IARC working group reviewed the evidence for processed meats. We present this information as auxiliary data, as processed meats are a subset of foods of interest in relation to nitrite exposure. However, the monograph on the 2015 IARC working group's has not yet been published. The OEHHA

team that developed the HID had only an article by Bouvard et al., published in the Lancet, which summarizes the working group's findings. They classified consumption of processed meats as carcinogenic to humans, that is Group 1, based on sufficient evidence of colorectal cancer.

For studies of nitrite exposure published since IARC's 2006 review, we've created a severe of data displays, such as the one shown here. These are called forest plots. First, before going through the data, I'd like to orient you, those of you who are unfamiliar with these kinds of plots, to this sort of data display, as I'll be showing several of these during my presentation.

The first column on the left shows the name of the authors of the study; that is, the source of data. The second column shows which endpoint, what kind of health outcome we are looking at in this plot. The third column describes the exposure that was evaluated in relation to this health outcome. In the example in the first study, Miller et al. reported nitrite exposure only in combination with nitrate exposure, and their estimated intake comes from processed meats in participant's diet. The second study reported on all dietary nitrate.

The fourth column from the left shows the

estimated level of nitrite. The units vary by study, generally either micrograms per thousand kilograms -- kilocalories of diet or milligrams per day. For each endpoint, exposure level increases as you move down the page within each study. The lines plotted to the right of that column show the estimated risk from exposure at that level, with the point estimate shown by a dot and a confidence interval shown by the line. The dotted line that runs vertically on the plot and is highlighted in this slide indicates a risk of 1.0, which reflects the null hypothesis of no increased risk. The three columns to the right of the plot list the numbers that are plotted for case control studies, the odds ratio, and the upper and lower bounds of the confidence interval.

Now, regard to these data, we are looking at two case-control studies that examined nitrite exposure in relation to colon cancer. Because all of the exposure lines have confidence lines that intersect the dotted line at 1, we know that none of these group had increased risks that are statistically significant. The risks of those in the first study are generally greater than one and appear to increase with increasing exposure levels, but all the confidence limits cross the dotted line.

So the second study, you may notice that we have

data for two colon cancer subsites. In this case, colon -- distal colon cancer appears to have a somewhat different pattern of risk compared to proximal colon cancer. We have included displays for subsites when that information was available.

There are four cohort studies that looked at colon cancer. You'll see that the second shown but Loh et al reported risk only in relation to a measure of continuous exposure, with the risk in this case not being significantly increased, but I just wanted to point out that this type of exposure measure is per milligram per day as a continuous variable, or half a milligram per day in this case.

The fourth study listed DellaValle et al, which looked only at woman, found significantly increased risk of colon cancer in relation to intake of preserved foods, although there is not a trend of increasing risk with increasing exposure.

The case-control studies of rectal cancer shown in this plot include one study conducted by Zhu with significantly elevated risks in the third of four exposure categories, a risk of 1.51. No increased risks were seen in the other case-control study that reported only nitrite plus nitrate.

In the cohort studies of rectal cancer, three of

the four studies show some indication of increased risks, but none are statistically significant. The DellaValle study, which you may recall found increased risks for colon cancer, did not find similarly increased risks for rectal cancer.

Some studies also reported a risk estimate for colon and rectal cancers combined, including the four case control studies shown here. One interesting aspect of the Ward et al study is the comparison of risks based on nitrite intake from published values; that is, levels of nitrite as reported in the published literature, to levels of nitrite these investigators measured in food, in processed meat in this case. Both subsets of the Ward study show elevated risks, although none are statistically significant. The other three case-control studies do not show an indication of increased risk.

The three cohort studies that looked at combined colon and rectal cancer show some indication of elevated risks, but none of these were significant.

Moving now to esophageal cancer.

IARC reviewed two case-control studies of esophogeal cancer, both of which had positive nonsignificant association with nitrite intake. In their review of the two-case control studies, Jakszyn and Gonzales considered the data insufficient. In

studies published since IARC's review, two cohort studies and one case-control study looked at all esophogeal cancer endpoints combined. The study of occupational exposure by Xie et al found significantly elevated risks. This was an exposure to sodium nitrite. The case-control study by Ward, et al, shows some indication of increasing risk with increasing exposure to nitrite plus nitrate from animal sources, but the risks were not significantly increased.

Two cohort studies looked at subsites of esophogeal cancer. For esophogeal adenocarcinoma, only the risk at the highest dose in the Cross et al study shows any indication of an increase, and this was not significantly increased.

For esophogeal squamous cell carcinoma in these same two cohort studies, there is some indication of increasing risks with increasing exposure, particularly in the men in the Keszei et al study. The measure of continuous exposure was significantly increased in this group.

Turning now to stomach cancer.

IARC and their 2010 monogram found a positive association in six of seven case-control studies that was significant in four. There were two cohort studies, including a Finnish study that found no association, and

a Dutch study that found a significant increase in risk for the highest intake. Based on these data, IARC concluded that nitrite in foods is associated with an increased incidence of stomach cancer and classified the overall human evidence as limited.

Jakszyn and Gonzalez in their 2006 review noted that the evidence supports a positive association with gastric cancer. Two meta-analyses that pulled relative risks across studies of ingested nitrate both reported similar risk level, though only one reach statistical significance.

Auxiliary information provided by the 2015 IARC working group on red and processed meats as summarized by Bouvard et al, noted that a positive association with consumption of processed meat was found for stomach cancer.

In the one cohort study that looked at all gastric cancer endpoints combined in the set since IARC's review, risks were not increased.

Two of the three case-control studies that looked at all gastric cancer found a indication of increased risks, particularly with animal sources of nitrite in the diet. Hernandez-Ramirez found significantly increased risks for those with higher intake levels, particularly for diffuse gastric cancer.

In the third study on this plot, Xu et al estimated exposure based on a one-time sample of urinary nitrite and compared those who were H. pylori positive with those who were not, finding a positive association with levels of nitrite in urine only in a small set of people who were negative for H. pylori. Infection with H. pylori is associated with stomach cancer. The study in the middle of this plot by Hernandez-Ramirez actually controlled for H. pylori status, which may be one of the reasons for the strengths of this study's findings.

Two cohort studies look at subsites of gastric cancer. Risks for gastric cardia adenocarcinoma were not elevated. Risks of gastric non cardia adenocarcinoma were not significantly elevated in these two studies, although the study by Keszei shows some indication of increased risks for men.

We now turn our attention to sites beyond the gastrointestinal tract, beginning with lymphoma. IARC, in their 2010 monogram, reported on two case-control studies of Non-Hodgkin Lymphoma, one of which found an increase in risk with increasing quartiles of nitrite intake. They noted that when plant and animal sources I of dietary nitrite were evaluated separately, the positive association was observed only for plant sources. A recent meta-analysis of four case-control

studies reported an elevated but not significant risk for highest versus lowest nitrite intake.

With respect to studies of Non-Hodgkin Lymphoma, published following IARC's review, there are four case-control studies, three of dietary exposure to nitrite and one of occupational exposure. Each of these four studies found some indication of elevated risks. The occupational case-control study conducted in Germany is not shown on the plot. This study found significantly elevated risks, but provided only results for exposure to nitrite, nitrate, or nitrosamine, and not nitrite alone.

Because of the many subsets examined in some of the dietary studies, the plots extend over three slides for lymphoma. Here on this plot, you see the study for Chiu et al, which looked at subgroups based on the presence or absence of a chromosomal translocation, t(14:18). In this study, those who had the translocation and consumed greater levels of nitrite had significantly increased risks of Non-Hodgkin Lymphoma.

In the Ashebrook-Kilfoy et al 2013 study shown below that, increased risks are seen in those with the translocation, but these are not statistically significant. This study included both men and woman and examined risks by gender as well as by source of dietary

nitrite. You can see on this plot that there does appear to be a difference in risks by gender, with women's risks higher than men's, and significantly increased risk for one exposure group in relation to nitrite from processed meat intake.

In the study that looked only at women published in 2010, Ashebrook-Kilfoy examined nitrite intake in relation to lymphoma subtype and sources of nitrite in the diet. For follicular lymphoma, shown on the plot as FL, risks increase was increasing nitrite intake from all sources, and the highest exposure group has significantly increased risks.

For those with the diffused large B-cell lymphoma, shown on the slide as DLBCL, the midrange but not the highest intake group had significantly increased risks in relation to nitrite intake from all sources and animal sources.

In this same study, for the subgroup with chronic lymphocytic leukemia or small lymphocytic lymphoma, abbreviated as CLL/SLL, there are significantly elevated risks for both the low and high intake group in relation to nitrite from plant sources. There was also a cohort study not shown in the plots that looked at lymphoma subgroups, Daniel et al, and they found an indication of elevated risks for those

with CLL/SLL, but no trend with increasing exposure.

Back to the case-control studies shown on the plot. There are also significantly increased risks for those with T-cell lymphoma in relation to all source and animal source of nitrite in the diet, but no indication of increasing risks with increasing exposure.

Turning now to brain cancer. For this and the rest of the sites, we do not have results displayed on plots.

IARC examined brain cancer in relation to two different types of populations, children and adults. Although IARC did not mention brain cancer in their overall finding, they summarized their evaluation of evidence in these population, excerpts of which are shown here.

Following their evaluation of 12 case-control studies of childhood brain tumors, they noted in relation to maternal diet, that children born to mothers who had the highest category of intake of nitrites specifically from cured meat, had an almost twofold increased risk for brain tumors.

In relation to maternal exposure to nitrite via drinking water during pregnancy, IARC noted there was a twofold increase in risk for brain tumors in the offspring in relation to nitrite levels in residential

drinking water, and that this effect was stronger among woman who did not rely on bottled water.

IARC also examined seven studies of dietary nitrite exposure in adult brain cancer. No significant associations were reported for dietary nitrite intake overall; however, in the largest study that was conducted in California, IARC noted that researchers observed a twofold increase in risk among men who consumed level of nitrite above the median and level of vitamin C below the median. There were also two studies -- two small studies with a positive association between adult brain cancer and intake of nitrites from cured meat. Also, a larger case-control study found threefold increase in adult brain cancer among those with high consumption of nitrite from plant sources.

There have been two cohort studies of dietary nitrite and adult brain cancer published since IARC's review. One found elevated but not significantly increased risks in relation to total dietary nitrites intake. The other found significantly elevated risks from nitrite -- with nitrite from plant sources. The highest intake level in men in the second study was associated with a twofold increased and risk, and the trend of increasing risks with increasing exposure was also significant.

These investigators also looked at diet during adolescence, estimated by study participants retrospectively, and found that risks were elevated for the fourth of five exposure categories; however, this was for nitrite plus nitrate. And in contrast to the findings for adult exposure, there was no trend with increasing exposure during adolescence.

A recent metaanalysis that looked at two cohort studies and four case-control studies of adult brain cancer reported a statistically significant increased risk when comparing lowest versus highest exposure level.

Turning now to thyroid cancer. IARC did not mention thyroid cancer in their 2010 monograph. The two cohort studies that we evaluated published since IARC's review were led by the same author but looked at different populations. Ashebrook-Kilfoy's 2011 study looked at men and woman in six U.S. states, and they found an elevated trend for follicular thyroid cancer in men.

The 2013 publication look at women only in Shanghai, and reported significantly elevated risks for all source and processed meat source nitrite intake with a significant trend for the processed meat intake.

In a review published in 2014 that looked at

three cohort studies, the authors noted that dietary nitrite and nitrate showed a positive association with thyroid risk. Two recent meta-analysis estimated a very similar relative risk using the available studies, and these risks of thyroid cancer in relationship to dietary nitrite were significantly increased.

Finally, other cancers. IARC 2010 reviewed studies of dietary nitrite intake in case control of cohort studies in relation to a number of other sites, and noted that the number of studies of any given cancer site were few with, for example, three case-control studies of pancreatic cancer and two or fewer studies of cancers and other sites.

In our review of studies published since IARC's review, we found that there were positive endpoints seen for dietary nitrite exposure in relation to several of these endpoints in some but not all studies, and a few endpoints were examined for which no positive studies were found.

In summary, a large number of epidemiologic studies, more than 100, have examined the association between dietary nitrite exposure and cancer at a variety of sites. IARC in their 2010 monograph concluded that nitrite in food is associated with an increased incidence of stomach cancer. This conclusion was based

on seven well-designed studies. With regard to brain cancer, the working group noted a increased risk in children born to mothers with the highest category of intake of cured meats and increased risks in adults. They noted that with the exception of stomach and brain cancer, few case-control or cohort studies are available for any given cancer site, and they classified the overall evidence as limited.

In the ten years since that review, the many additional studies conducted add colon cancer, Non-Hodgkin Lymphoma, and thyroid cancer, among others, to the list of sites of possible concern.

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DR. HSIEH: So I will continue on with evidence from the study in animal. The 2010 IARC monograph evaluated 55 animal cancer bioassay that test nitrite in combination with either fishmeal, a complex mixture of amine and amide, or nitrate in combination with individual amine or amide. That concludes there's sufficient evidence in experimental animal for the carcinogenicity of nitrite in combination with amines or amides.

OEHHA identified an additional 35 animal bioassays of nitrite in combination with amines or amides. Findings from all 90 of this study presented in

table in OEHHA's Hazard Identification Document. Table 9 presents cancer bioassay of fish meal in combination of amine and amide. Table 7 presents cancer bioassay on 23 individual amine in combination with amides or in combination with nitrites. Table 8 present cancer bioassay on 15 amides in combination with nitrite. Increase in tumor incidence were observe in members of this study, with tumor occurring at multiple sites and in multiple Leiden species and strains.

Here is the information on study design and study finding from the two study of fish meal administered in diet in combination with sodium nitrite, administered in the drinking water for two years to male and female Fischer F344 rats. In each study, animal received either fish meal alone or fish meal plus sodium nitrite. In each study fish meal was administered at three dose -- 8 percent, 32 percent, or 64 percent of the diet. Intake of sodium nitrite in drinking water increase with increasing label of fish meal in the diet.

In male rats, a statistically significant increase in rare kidney adenoma, and adenocarcinoma was observed in the middle and high dose group receiving fish meal in combination with nitrite compared to the group receiving fish meal alone.

In female rats, a statistically significant

increase in rare kidney adenoma was observed in the high dose group receiving fish meal in combination with nitrite compared to the group receiving fish meal alone.

In addition, rare uterine adenoma and adenocarcinoma were observed in middle and high dose female receiving fish meal in combination with nitrite, while no uterine tumor were observed in female administered fish meal alone.

Because of a large number of animal cancer bioassays combined with individual amines or amides in combination with nitrite, we cannot present it now. Please refer to our document for more detailed information on cancer bioassay study design and study finding, which are presented in table 7 for amines and table 8 for amides.

In the following presentation, we will show one or two examples from study of nitrite in combination with amine and study of a nitrite in combination with amides to highlight some carcinogenicity finding for your reference.

Before I present some example finding from animal cancer bioassay, maybe explain how we evaluate the study finding. For our purposed today, the test group of interest is the group test with nitrite plus amine or amide. There are three comparator group: the

untreated or vehicle control group, a group treated with nitrite alone, and a group treated with amine or amide alone.

Study are -- were described as positive if a increase in tumor instance in the test group were statistically significant or biologically significant in the case of rare tumor as compared to all comparator group.

Study were described as inconclusive if increase in tumor incidence in the test group were significant, but definitive conclusion are not possible since the study lacked one or two comparator group.

Study were described as negative if no significant increase in tumor instance was observed in the test group compared to at least one comparator group.

Next slide shows the finding from cancer bioassay in male with high rates of secondary amine with hydroxypropyl amine paired in combination with nitrite. This study has a control group, a group receiving only nitrite alone, a group receiving only the amine, and a group receiving the amine in combination with a nitrite.

This study report positive findings, specifically the instance of a rare nasal carcinoma, rare nasal papilloma and lung papilloma. Shown

statistical significant increase in the test group as compared to all three comparator group. Rare tumor the esophagus and lung were also observed in the test group, while none occurred in the comparator group.

Here's is another set of example of animal bioassay of morpholine a cyclic -- secondary amine test in combined with nitrite in study in mice, rats, and hamsters.

In Swiss mice, positive finding the lung adenoma were observed for morpholine in combination with nitrite. In Sprague-Dawley rats, positive finding of a lung angiosarcoma, liver carcinoma, and liver angiosarcoma were observed.

In Syrian golden hamsters, positive finding of a liver carcinoma were observed; therefore, more finding in combination to nitrate induced tumors in mice, rats, and hamsters; and in rats, tumors were induced at multiple sites.

This slide present a summary of the result from the animal carcinogenicity study of nitrite tested in combination with 23 individual amines. The left column the different subtype of amine from top to bottom, noted like some amine are members of multiple amine subtypes. For example, IQ and PhIP is a primary amine, a tertiary amine, and a cyclic aromatic amine.

The next column indicates the number of amine of that subtype that have been tested. The remaining column to the right indicates the number of amines that have positive tumor finding, inconclusive tumor finding, and negative finding. The name of the specific amine tested and found to be positive, inconclusive, or negative was shown here for your reference. For example, 11 secondary amines have been studied in animal cancer bioassay. Four have positive finding; three have inconclusive finding because the study lack one or more comparator group; and four have negative finding.

Similarly, 13 tertiary amine have been studied. Three have positive findings; three have inconclusive finding, and seven have negative finding.

Now moving on to example of amide tested in combination with nitrite and cancer bioassay. Here is the example of the study of dodine or guanidine test in combination with nitrite in studies in mice. Findings from study of exposure to pregnant indicates here as F-0 females, and study of in utero exposure indicates here as F-1 males and F-1 females.

Positive finding of a lymphosarcoma were observed for dodine in combination with nitrite for F-0 females, F-1 males, and F-1 females.

This slide present a summary of the results from

the animal cancer bioassay study in combination of nitrite with 15 individual amides. The left column leads to different subtypes of amide from top to bottom. Notice that some amides are members of multiple amide subtypes. For example, allantoin is both of secondary amide and also a urea. The table here is arranged like the previous amines summary of -- table. For example, seven urea has been studied in animal cancer bioassay. Five have positive findings, nine have inconclusive findings, and two have negative findings. Similarly, four guanidine have been studied -- what's going on? No screen. Yeah, we lost the screen. Should I continue? We cannot see the --

CHIEF COUNSEL MONAHAN CUMMINGS: Can you see it? It's on your screen.

DR. HSIEH: I can -- this side and we wait for they -- come to fix the monitor, or should I just continue?

CHAIRPERSON MACK: Anybody have any questions for Dr. Hsieh?

COMMITTEE MEMBER EASTMOND: We see -- we have the presentation on, but it's not projecting behind us.

CHAIRPERSON MACK: Oh, I see.

DR. HSIEH: Yeah, not the monitor, so the public cannot see it.

COMMITTEE MEMBER EASTMOND: Even though the audience can't see it, but we can see it.

CHAIRPERSON MACK: Well, I don't know what the alternative is.

COMMITTEE MEMBER EASTMOND: Probably continue.

CHAIRPERSON MACK: Do you have any suggestions to an alternative? My inclination is to go ahead.

DR. HSIEH: Okay. Okay. Thank you.

So four guanidine have been study. One have positive finding, two have inconclusive finding, and one has negative findings.

Moving on to the next slide. Next slide. Yeah. This slide present a summary of target tumor sites observed in animal carcinogenicity study of nitrate in combination with either fish meal or amine or amide. So study conducted in rats, mice, and hamster.

Now moving on to mechanistic evidence and other relevant data. Mechanistic evidence reviewed by IARC include information on nitrosation reaction. In this reaction, nitrite react with amine and amide to form -- sorry -- to form a nitroso compound such as nitrosamine and nitrosamide. In nitroso compound, can react with DNA to cause DNA damage. This DNA damage can result in tumor formation.

IARC also reviewed the genotoxic effect of

nitrite alone. In IARC review, positive finding of a genotoxicity induced by nitrite include the induction of chromosomal aberrations and micronuclei in vitro and in vivo. Aneuploidy in Syrian hamster embryo cell in vitro. Multiple type of mutation induced in vitro and in animal exposed in utero, and mouse sperm-head abnormality induced in vivo.

OEHHA supplemented IARC's review of the genotoxicity of nitrite alone with a review of genotoxicity study of nitrite in combination with amine or amide.

OEHHA identified genotoxicity study with nitrite test in combination with 111 different amine and 39 different amide. Findings from this study are presented in tables in OEHHA Hazard Identification Document. Table 10 presents genotoxicity study of a nitrite in combination with amine. Table 11 present genotoxicity study of nitrite in combination of -- with amide. Positive finding have been observed in a number of tests of this study. Using a number of different test systems, including bacterial, yeast, mammalian cell in vitro, and rodents in vivo.

The genotoxic endpoint assessed in this study with positive finding include DNA mutation, DNA damage, gene conversion, DNA strand breaks, and unscheduled DNA

synthesis. Because of larger number of genotoxicity study of nitrite in combination with amine or amide, we cannot present at OEHHA now. Please refer to table 10 and 11 in OEHHA's document for more detailed information on genotoxicity study design and study findings.

In the following presentation, we will show examples from study of nitrite in combination with amine and from study of a nitrite in combination with two amides to highlight some genotoxicity finding for your reference.

Before I present some example finding from the genotoxicity study, let me explain how we evaluate the study finding. Like animal cancer bioassay, the test group of interest is the group tested with nitrite plus amine or amide. The three comparator groups are untreated or vehicle group, or a group -- sorry -- or a group test nitrite alone, and a group test with amine or amide alone.

Study are described as positive if more than twofold increase in genotoxic effect was observed in test group as compared to three comparator groups. Studies were described as inconclusive if more than twofold increase in genotoxic effect was observed in test group. The definitive conclusions are not possible since the study lack one or more comparator group.

Study was described as negative if no increase or less than twofold increase in genotoxic effect was observed in the test group compared to at least one comparator group.

This slide shows the finding from five genotoxic studies of secondary amine, dimethylamine tested in combination with nitrite. The first three studies are salmonella G46 host-mediated assay conducted in vivo in mice and rats. The fourth study is more combinational salmonella reverse on mutation study. And the fifth study assessed vivo DNA's break in male rats exposed in vivo. The first full study include a test group and all three comparator groups. The fifth study like it -- untreated control group. Positive finding are a observed in the first three studies. The fourth study is negative. The findings from the fifth study are inconclusive.

This slide presents a summary of result from the genotoxicity study of nitrite tested in combination with 111 individual amines. The tables low in column are arranged like the previous amines animal cancer bioassay summary table. The name of a specific amine tested and found to be positive, inconclusive, or negative are shown here for your reference. In some case, only a partial list is provided due to the space limitation.

Of 14 primary amine has been tested in combination with nitrite for genotoxicity. Four have positive findings, seven have inconclusive finding, and three have negative finding.

Of 48 secondary amine tested, 38 have positive finding, 7 have inconclusive finding, and 3 have negative finding.

Of 52 tertiary amine tested, 24 have positive finding, 19 have inconclusive finding, and 9 have negative finding.

One quaternary amine has been tested with negative findings.

Of 34 cyclic aromatic amine tested, 16 have positive finding, 8 have inconclusive finding, and 10 have negative finding.

Now, moving on to examples of amide test in combination with nitrite for genotoxicity. Here are example of genotoxicity study of two urea compounds -- ethylurea and methylurea tested in combination with nitrite. The study of ethylurea is salmonella G46 host-mediated assay conducted in vivo in mice. So is the second study of methylurea. Both of these host-mediated assays include a test group and all three comparator group, and both reported positive finding of amine toxigenicity.

The first methylurea study of DNA of strand break in Chinese hamster ovary cells in vitro, like the untreated control; therefore, the finding are inconclusive.

Next slide presents a summary of the results from the genotoxicity study of nitrite tested in combinations with 39 individual amides.

The tables shown low in the column are arranged like previous amides animal cancer bioassay summary table. For example, six urea has been tested in combination with nitrite for genotoxicity. Three have positive findings, one have -- has inconclusive finding, two have negative finding. Similarly, four guanidine have been tested. Two have been positive findings, two have inconclusive finding, and none have negative finding.

So to sum up the evidence from animal cancer study of nitrite in combination amines and amides, IARC reviewed 55 cancer bioassay, and based on that review, concluded there is sufficient evidence in experimental animals for the carcinogenicity of nitrite in combination with amine or amide. Considering all 90 cancer bioassay present in table 7, 8, 9, of OEHHA's Hazard Identification Document, positive findings were observed for nitrite in combination with fish meal in

two studies in rats. In male rats, statistically significant increase in rare kidney adenomas and adenocarcinoma were observed. In female rats, a statistically significant increase in rare kidney adenoma was also observed, along with observation of rare uterine adenoma and adenocarcinoma. Possibly a tumor finding were also observed with nitrite in combination with seven individual amines and for nitrite in combination with seven individual amides.

Inconclusive findings were observed for studies with eight amines three amides. Negative findings were observed for studies with 13 amine and 5 amides.

To sum up the evidence from genotoxicity study of nitrite tested in combination with amine and amide. Positive genotoxicity finding were observed in at least one assay for 59 amine and 15 amide tested in combination with nitrite. Of 59 amine with positive genotoxicity finding, four are primary, 38 are secondary, 24 our tertiary, and 16 are cyclic aromatic amine. 15 amides with positive genotoxicity finding, four are primary amides, one is a secondary amides, two are tertiary amides, three are urea, one is carbamate, three are sulfonamides, and two are guanidine. Inconclusive finding were observed for 36 amines and 20 amides. Negative findings were observed for 16 amines

and four amides.

For the chemical list in carcinogenic finding, please refer to table 12 and 13 in the Hazard Identification Document, which it summarize the genotoxicity and animal carcinogenicity finding for each of the individual amine and amide tested in combination with nitrite. The table also grouped each of the amine and amide by subtype.

With that, conclude today's presentation, and thank you.

CHAIRPERSON MACK: Jennifer and Martha and Amy, you did a fantastic job on summarizing what was a really voluminous set of reports and data. I compliment you on that. I'm not sure how good it's going to do in the long run, but you did a terrific job.

Now, our job is to decide whether or not we should list nitrites in relation to amides and amines as a general category, and so I would ask now -- I would like to take a slightly different tact than usual. Usually we started with the epidemiologic data, but I would rather start with the -- first of all, I guess we --

PUBLIC MEMBER: Mic is not on.

CHAIRPERSON MACK: What's wrong, guys?

ACTING DIRECTOR ZEISE: It's working now.

CHAIRPERSON MACK: It was working before, it just wasn't close enough.

Do we have any questions for clarification for Jennifer or Amy? Bill.

COMMITTEE MEMBER LANDOLPH: Again, I have comment that you did a masterful job on all issues. I had a couple of questions. The first one is, I was going to ask you right away, what were the percentage of amines that were positive, and I'm looking at this data right in front of me. So if you have 59 amines, and you've got -- let's see -- 59, and we've got 20, which are negative -- oh, 16 negative, and 36 inconclusive, so that's 42 out of 59 are inconclusive or negative. So it's putting us in a little bit of difficult position to give a blanket and premature that we could accept all of them right away, is what I was thinking to begin with.

Do you have any idea as to structural considerations in the amines that might -- obviate listing them -- do you have any reason why they would be negative or inconclusive?

DR. SANDY: It would take more digging and serious thought to come -- no easy patterns were apparent. We've laid out the studies and provided the original studies to you, and we'd have to look, but we didn't see any clear patterns. I would point out that

the negative studies, you know -- as you know, we're just reporting what's out there. That may be one test and it's negative or one test and it's inconclusive because it's missing a comparator group.

COMMITTEE MEMBER LANDOLPH: And I've seen it structurally -- I teach some of this each year in a carcinogenesis course. You need an alpha carbon with a hydrogen that can get metabolized by the T450 to result in the formation of nitrosamines, so maybe you could rule out some there in crafting the legislation for this more precisely is what I'm thinking.

CHAIRPERSON MACK: Anymore questions? All right.

MR. MURRAY: Thank you, Chairman Mack, and good morning. Jay Murray commenting on behalf of the California League of Food Processors, the California Retailers Associations, the California Grocers Association, the Western Agricultural Processors Association, the California Chamber of Commerce, the Grocers Manufacturers Association, and the North American Meat Institute, and thank you for reading our written comments.

I suspect this topic may be the easiest part of your day. Nitrite in combination with amines or amides is, as you know, an unusual topic for your agenda, and

the first of those is why it's on your agenda at all, and you've heard a little bit about this. It's -- unlike most compounds that come before you, this is not on your agenda because it was assigned a high priority, and it certainly wasn't a conclusion of OEHHA that this is a compound or class of compounds that should be listed. The only reason these combinations are on your agenda today, as has already been noted, is because of a peculiarity in the regulations on authoritative bodies.

The authoritative bodies listing regulations requires that where chemicals are considered and rejected for listing under that mechanism, it must be referred to the States qualified experts, which is you, and Dr. Sandy made the point right at the outset of this meeting. In other words, OEHHA had no choice but to refer to ask your committee whether, in its opinion, the chemical nevertheless meets the more rigorous clearly shown to cause criteria.

In this case, OEHHA's conclusion was that nitrite in combination with amines or amides could not be listed via authoritative bodies because, quote, the evidence is limited to a comparatively small number of chemicals. For the same reason that OEHHA determined nitrite in combination with amines or amides could not be listed under authoritative bodies mechanism, this

broad class cannot be listed under the clearly shown to cause listing criteria either. And there can be a little doubt on that subject. In fact, although such a listing would cover tens of thousands of compounds, and an even larger number of products, the fact is that the comments I coauthored are the only comments the Committee received. No one has advocated, at least not in writing, that the listing of this broad category or any subset of this category should proceed at this time.

Nitrite in combination with amines or amides is a broad ill-defined class of tens of thousands of possible combinations, some known, some unknown, and only a handful have been tested for carcinogenicity. You heard that of the 38 combinations tested for carcinogenicity in animals, the HID identified only 14 with at least one positive test. So of the tiny minority that were tested at all, the majority were not positive; and, moreover, the combinations tested first were thought most likely to yield positive results. They weren't selected randomly.

Finally, even the so-called positive animal study or test for the 14 positive combinations may not withstand scientific scrutiny. For example, the animal evidence of carcinogenicity for one of the 14 positives chlorpheniramine, the antihistamine drug in combination

with nitrite, was limited to one tumor type, liver; in one sex, males; in one species, rats; in one study, a study which is unlikely to qualify as scientifically valid testing.

Importantly, those reportedly positive results do not reflect a pattern or a mechanism of action that has application across the entire category of nitrite in combination with amines or amides or any significant subcategory. There's even less epidemiologic support for listing nitrite in combination with amines or amides. There's not a single epidemiologic study of nitrite in combination with amines or amides, and both Dr. Sandy and Dr. Dunn acknowledge that the epidemiology studies which you saw were studies of estimated exposure to nitrite, not estimated exposure to amines or amides.

So in conclusion, nitrite in combination with amines or amides does not meet the listed criteria because the evidence is limited to a comparatively small number of chemicals. Ten of thousands of combinations cannot be clearly shown to cause cancer based on positive results with only 14 combinations at most.

Thank you. I'd be pleased to answer any questions.

CHAIRPERSON MACK: Thank you for being succinct and clear, Jay. Anybody have any questions for Murray?

Okay. Let's take a five-minute break.

(Brief recess was taken.)

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CHAIRPERSON MACK: I'm going to ask the folks who have -- I'm going to change the order that we usually do and discuss the epidemiology or at least address the epidemiologic issue after we address the animal data and chemical information. So the first thing I'm going to do is ask Dr. Eastmond and Dr. Bush and Dr. -- and Joe to give us their opinion on whether or not we should list the combination of nitrites and the whole category of amines and amides, and then we'll take a vote about that. And then we'll discuss whether or not we have any suggestions for how we might proceed by altering the -- the rubrics to do something useful.

So, again, I will say we are going to have Dr. Landolph, Dr. Eastmond, and Dr. Bush each address the -- on the basis of the animal data and carcin -- and the -- and the chemical data they've looked at, on whether or not they're in favor of listing this category of nitrite plus the rubric -- total rubric of amines and amides. Then Dr. Reynolds and I will do the same for the -- based on the epidemiology information in light of what they've said, and --

ACTING DIRECTOR ZEISE: Mechanistic.

CHAIRPERSON MACK: Mechanistic, thank you. I didn't have the word mechanistic in my mind. Now I got it firmly ensconced, at least for the next five minutes. So is that clear?

All right. So let's start with Dr. Eastmond.

COMMITTEE MEMBER EASTMOND: Is this on?

PUBLIC MEMBER: No, not on.

COMMITTEE MEMBER EASTMOND: We know this one works. Okay. So I was asked to review -- to discuss and review the animal cancer bioassays associated with the combination of nitrate -- nitrite plus amines, okay. And the challenge is -- is alluded to, and Jay mentioned this, you've got a class of probably thousands of chemicals, and you only have animal bioassays for a small subset of these. And within those animal bioassays, you get a real sort of mixed series of results. So by my sort of judgement or conclusion, there were somewhere 22 to 23 total amines, which were evaluated. Based on the evidence we've seen, probably three of these may have sufficient evidence depending on -- and another two might have probably sufficient evidence depending on how they are describe; another four have some evidence; and then the -- I would say the majority or certainly 13 of these I would consider inadequate evidence, okay. So as a group -- and I can

go through those specifically if people are interested -- but, in essence, you have a very broad category. We have data for only a small subset of these, and even in those, we have data -- only a very small subset of these, really, I would think, would have sufficient evidence that one way consider listing them. And what my concern would be is if you cast a broad net, you are going to catch lots of things which are not carcinogenic and would label -- list them as well, so that would be the concern.

Do you want me to address genotoxicity at this point? Okay. So in a similar sort of thing with the genotoxicity. There are a lot of positive results in a lot of cases -- well -- so I look at this and sort of crudely probably 40 percent of the chemicals tested showed positive results; about 30 percent were inconclusive; another 30 percent there was no sort of interaction between these.

Now, one of the challenges is the genotoxicity test, the chemicals test for genotoxicity in some cases overlap with those tested for animal cancer bioassays, but many cases, they don't overlap, so they are a total different section, so we don't know what -- if they would cause cancer or not. Genotoxicity tests are screening tests to help us make decisions, but they're,

in my mind, insufficient to make a decision as far as Proposition 65. So they're informative, again. So it's a broad class. There some here that look like -- clearly genotoxic, a group that are inconclusive, and a group that are basically in which there's inadequate or no evidence for genotoxicity. So, again, it's a very mixed sort of bag. It's very hard to draw specific conclusions, and I didn't see obvious ways of classifying these among the amines. Now, there may be something we can -- Jason might -- talk about some of the possibility -- possible classification in that group -- amides, but that's it.

CHAIRPERSON MACK: I'd rather hold off for a moment. Jason, go ahead.

COMMITTEE MEMBER BUSH: Thank you. I'll start off by saying I did read the public comments and the public comment document from the collective organization, and you make several logical arguments in that document.

My charge was to evaluate the relationship between nitrite and amides. And just to recap a little bit about what was already talked about, of the approximately 15 amides that were evaluated, seven of them showed positive tumor findings. And of those seven, five were ureas. It's interesting that when I

take a macro view of those -- of that information, of those amides studies with positive tumor findings, we see a mixed bag of tumors. We see some rare tumors. We see benign and malignant tumor types as well. We see that across species, different rodents, both rat and mice; different strains; and in males and females. There are mixed ages involved. There's obviously some in utero exposure as well. There are mixed roots, either through drinking water or intergastric gavage, feeding them or through the chow. So it's difficult to make a collective decision over this entire class. I mean, considering all amino acids fall into amides, it's -- it's questionable.

While most of the studies utilize single doses, they are well below the LD fifties and subchronic treatments, so -- and there's a little bit of dose response there, but when you compare that to the controls, there's certainly a clear and strongly significant difference with looking at these particular amides that were positive in conjunction with nitrite as a group compared to the controls.

I find that I have to align myself with the conclusions from the IARC 2010, and I do find that there is sufficient evidence in animal carcinogenicity for those amides that were evaluated and show positive tumor

findings.

CHAIRPERSON MACK: Joe.

COMMITTEE MEMBER LANDOLPH: Yeah, I agree with everything that Jason and David already said. I just had a couple more thoughts. One is, what you are actually trying to do here is look at nitrosamine formation, and that's not what's being measured, you know, in the new you -- that's being studied, via animal blood or whatever, so this is a surrogate for that. And the rate constant for that would be a constant times the -- concentration nitrosamine times the concentration of the amine, times the concentration of the nitrite, or whatever the nitrite leads to, which is supposed to be the nitro-saving agent, and that's not clearly worked out. So there's some more mechanistic work that has to be done here, so I think that could be sharpened up. I guess my points at this time would be pretty much what Jason and David said. Those -- some of those compounds really trumped up traumatically. When you added nitrite alone, there was nothing. When you added the amine alone, there was nothing. When you added the two together, there was a 25 to 100 fold increase. So clearly this goes to being linked together to make a nitrosamine is the key, and I think that's what we ought to stick to, and I'll suggest in the next session what I

think you might do.

CHAIRPERSON MACK: All right. Thanks, Joe.

My task was to looking at colorectal cancer and lymphomas, and that's pretty easy to do. I guess the first thing is that all of the epidemiologic studies are based on estimates of exposure, which are mixed in the extreme and based, oftentimes, on food frequency and consumption and interpretations of food frequency, which in turn is based estimates of content and food-specific content that comes from very specific sources and don't necessarily mean they are very accurate across the board. So whereas, if you look at the data for both colorectal cancer and for lymphomas, you get the feeling there probably is something there, but what the something is and what it's due to is very difficult to say. It's undoubtedly probably due to the combination of nitrate and some amines and/or amides in certain circumstances, but there is very little in the way of dose response and there's very little in the way of consistency from study to study or from subset to subset. So I would not be able to conclude that there was a potential for listing of the category nitrites plus amines and amides base on colorectal cancer or lymphoma. Peggy.

COMMITTEE MEMBER REYNOLDS: I could just agree,

or since I was signed all the other cancers, I might just mention, I think as has been well pointed out, the epidemiologic literature pretty much relies, for the most part, on dietary studies, and most of those dietary studies are food frequency questionnaire studies. With all of the inherent problems for that particular study design, I think it's worth mentioning that the IARC in 2010, the working group define the agent of interest as ingested nitrate or nitrite under conditions that result in endogenous nitrosation, so I think that it's very difficult from the point of view of looking at estimated exposures in the epi studies to really say what might be going on in the context of nitrites in the presence of amines or amides.

So there are few studies out there also that looked at water as a source of exposure, but that's primarily a source of exposure for nitrates and not nitrite, per se, so very little in terms of that. Specifically, a few, as was mentioned, was some biologic measurements, and most of the studies really tended to take a look at this exposure in the context of cured meats. And as we know, the new IARC monograph 114 that is soon to come out has specifically addressed the issue of cured meats.

So since the IARC monograph, there's sort of key

studies that have tried to address this have tended to be cohort studies, which of course are studies that IARC also gives more -- a little more weight to, and are studies which have attempted to do adequate adjustment for smoking, which is also tobacco smoke also as source of a number of these agents, and some more sophisticated dietary information usually with adjustment for vitamin C so that studies that seem to find associations tended to be those with very high nitrate intake and very low vitamin C intake in keeping with the whole view of the mechanism.

So since the IARC report, sort of the two studies that have seemed to address a number of the cancers, since some of these papers address several cancers and not really one cancer at a time, have tended to be EPIC, which is the European investigation into cancer nutrition, which is a very large study of half a million people from ten countries throughout the world, is really focused on trying to take a look at dietary factors and cancer. And in the U.S., the AARP, associate of the Americans retired -- retired cohort diet and health study, which is a large NCI sponsored cohort study, again, of over half a million older Americans, which was specifically designed, again, to try to take a look at dietary factors in cancer

outcomes. So a number of -- it's probably the most compelling evidence, I would say, for any cancer is that for stomach cancer, as was -- and as was cited in the IARC monograph in which they found limited evidence in humans for carcinogenicity of nitrite in food, and nitrite in food is associated with an increased incidence of stomach cancer. They reported on several studies, mostly indications to positive associations, mostly case-control studies, and then subsequent to publication, there were of course some more case-control studies, some null, some positive. And in the big cohort studies, AARP saw no association with nitrite values for processed meat, and the EPIC study was the Norfolk, the Cambridge portion of that study, so no association for overall dietary intake. And the Netherlands' cohort study saw no associations for nitrite from processed meat after adjusting for a number of factors, including smoking.

So for esophageal cancer, the evidence is rather mixed, as has been very nicely already reported to us. The three cohort studies that have been reviewed, only two have really looked at intake of processed meat, and together it's been somewhat equivocal, some suggestion of a higher risk for esophogeal squamous cell carcinoma, but not adenomacarcinoma. It's among men but not women.

And the Netherlands' cohort study, it's a rather mixed bit of evidence. There was suggestibly higher risks for both types in the AARP study, and no association in the EPIC study, the European study.

Brain cancer -- CNS and brain cancer is an interesting area, as has been pointed out. IARC reviewed a host of studies looking at childhood brain tumors, and what has been sometimes called the hotdog hypothesis. There was the big West Coast brain cancer studies and also the children's cancer study, a national study, which suggested higher level -- higher risks for mothers' consumption of processed meats during pregnancy, but not necessarily for children's own consumption. And since a number of these studies have been conducted, actually, vitamin C has been added to hotdogs, so the hotdog hypothesis hasn't really been that much further explored for childhood brain tumors.

The several studies of adult glioma that were perhaps inspired by some of these have been generally null. There was no association in an Australian study, a German study, an Israeli study, an Ohio study. No association in a Los Angeles study for general dietary nitrate, but a positive association for high levels from cured meat. Back to cured meat again. And in the San Francisco Bay Area study that was cited by Amy, there

was an increased risk for men, but not women, with high dietary nitrite intake and low vitamin C, so back to sort of that combination of ingredients.

Thyroid cancer, as it's been mentioned, is somewhat intriguing. IARC didn't address it in the 2010 monograph, but there have been two subsequent cohort studies that have suggested maybe something going on. The AARP cohort suggested an elevation in follicular thyroid cancer, which is a less common type and only in men, so in a pretty small subset of that cohort. And the Shanghai women's health study suggested elevations for dietary animal sources, processed meats, but not plant sources. So the thyroid cancer literature is very sparse and pretty uninterpretable.

Lung cancer, there's little evidence. IARC cited a couple of studies that suggested that there might be some association for men, but not women. In the Hawaiian study and in the Iowa women's cohort study, some association with intermediate average intake, but not actually measured intake or estimated intake. And, subsequently, there was no association in the EPIC cohort study, and not really in the Iowa Women's Health Study.

So stomach cancer, I already talked about.

What other cancers? There's many cancers and

very little to say. Breast cancer, there's very little evidence. There was no association, either in EPIC or the Iowa Women's Health Study. Head and neck cancers, no association in a finished case-control study, but a little elevation for nasopharyngeal cancer in a Taiwanese case-control study, and for oral cancers in a small Washington State study. Pancreatic cancer, there's been pretty much no evidence for risk. A series of null studies, both from IARC, and subsequently, no results from the AARP dietary study. Liver cancer, there's -- was not addressed in the IARC report, and subsequently, no association was observed in the AARP diet study or an ecologic study in Thailand. Ovarian cancer, a little suggestion from two recent studies, but again, sparse evidence. Bladder cancer, there was no association in two studies reviewing the IARC report.

Some suggestion from three more recent studies of elevation associated with consumption of processed meat, and in Los Angeles in a large well-known bladder cancer study in Los Angeles, there was a suggested elevation in never smokers, but not in ever smokers, again, addressing sort of the issue of covariants that may influence risks for these exposures in the human health studies.

Prostate cancer, no association in the European

EPIC study, and suggestion of increased risk in advanced, but not early prostate cancer with nitrite intake from meat in the AARP study. Only one study really tried to look at all types of cancer combined, the EPIC study, and found no association in their dietary study.

I think we had a very nice discussion of some of the meta-analysis and pooled analyses since the IARC report. Some have focused on the thyroid cancer issue, which looks interesting, but clearly the evidence is quite inconsistent.

A couple of reviews looking at stomach and esophageal cancer, again, suggest that positive associations for stomach cancer, little or nothing to say about esophageal cancer. And in the 2016 meta-analysis of 51 studies for various cancers. As already presented by Amy, we saw elevated risks for adult glioma and thyroid cancer, which is provacative but not necessarily borne out by extensive literature for the particular exposures of interest.

So, in general, I would say for the EPI studies, it's difficult to disentangle nitrate from nitrite exposures from the -- using food frequency questionnaire data. It's also problem for studies which specified processed meats as the source of exposure. Much as in

the case of the environmental studies dietary exposures to particular chemicals, of course, do not occur in isolation from exposures to other chemicals in the diet or in the environment.

I would say in general that the studies for all of these cancers published since the 2010 IARC monograph really do not change the assessment of IARC for group 2A, probably carcinogenic to humans, indicating that nitrate and food is associated with an increased incidence of stomach cancer.

With respect to exogenous amines and amides, so the good news/bad news is there's a lot of literature, which, in human health -- of human health studies, which try to address nitrite exposure, but really none, as it's been well pointed out, that address it in the context of the presence of amines or amides. We do know that cooking at high heat is known to be a source heterocyclic amines, particularly for cooked meats, and that is on IARC group 1 carcinogen. We do know that acrylamide, again, is formed cooking at high heat, french fries, and that is an IARC group 2A, which is limited evidence in humans and sufficient evidence in animals. But none of this has really been specifically addressed in the dietary studies, so it's hard to say what may be going on in the human health studies. The

preliminary assessment for monograph 114, implicating consumption of processed meat for colorectal cancer as a group 1 carcinogen. So, again, process meat may be high in nitrates, but also in nitrites, and also nitrates and other constituents, so I would say from the human health point of view, the evidence is quite limited, and I would -- I haven't seen anything in the more recent literature that would cause me to think of anything different than what was in the IARC 2010 monograph. That was a long way of say I agree.

CHAIRPERSON MACK: Anybody have any questions or is there any cross comments between individuals?

COMMITTEE MEMBER DAIRKEE: Thank you. My focus was basically the genotoxicity, and as my colleagues earlier just mentioned, that data is really all over the place. For a single chemical of all the different assays conducted don't even agree, but the problem that I really had with that data was the lack of positive controls. So if something ends up being negative, what does it really mean if there is no positive control in the assay? There was only one example of cimetidine with amines and amides where they did include MNNG as a positive control, so they were able to then confirm that cimetidine did not do what a known carcinogen did, a known genotoxic agent did. So that was a good

experiment, but that was the only one among the whole long, long, long table. But the one --

The one thing that I really found very useful in the HID was the comparison between animal data and the genotoxicity data. That was a very useful table 12. And from that table it appears that there's really only five chemicals where there's a positive match in terms of amines or amides increasing -- having an increased effect. So I think the Committee needs to have a closer look at some other future point as to those five chemicals, two of them -- and none of them are on the Prop 65 list.

So I think that's basically what I -- all I have to say about how convincing this data is.

CHAIRPERSON MACK: Thank you. We'll return to your five chemicals in a minute, but first, let's deal with the major issue right now. Does anybody have any questions for anybody else on the Committee? I'd just like to say that I agree with Peggy, the stomach seems to be the most likely candidate. And one of the things that convinced me was the contrast each time between the cardia of the stomach and the body of the stomach, suggesting that the same case-control dietary information was different for the two sides. But, again, I make the point that either with colorectal

cancer, there is a tendency for positivity all the time, but it's just never consistent.

Anybody have any other questions for anybody else? Okay. Let's take a vote.

COMMITTEE MEMBER EASTMOND: One thing -- I skipped over this when I was talking about the animal bioassays. For a couple of these, there are really striking increases seen in the combination of either the chemicals, amines, and the nitrites, so -- there so strong it's unlikely they're caused by any chance. I mean, they're very, very strong, but it's only for a limited number and it doesn't appear to be real consistency across classes, from what I can tell.

CHAIRPERSON MACK: Okay. I'll read the end of the sentence.

Has nitrite in combination with amines or amides -- actually, should be and/or amides, but I think that's being picky -- been clearly shown through scientifically valid testing according to generally accepting principles to cause cancer? So what we are going to do is ask for hands raised for the affirmative and then we'll ask for the negatives. So does anybody want to vote for a positive response to that statement?

I guess not. So let's put our hands up for the negative side. We fail to find evidence that there is

such an association, so we are finding all members were negative.

So I guess now we take a break for lunch, and we start with the others after lunch. What is the appropriate time limit -- yes, Peggy?

COMMITTEE MEMBER REYNOLDS: So that was for the broad class of everything, right? Do we or should we discuss specific --

CHAIRPERSON MACK: You are right. We should do that now. I want to start by saying, if I were going to design a way to try and educate the public and allow them to protect themselves against carcinogens when it comes to nitrite and amide and amines, this is not the very effective way. Listing is not the way to go, because we are going to wind up, I'm afraid, in the future listing foods, and foods are going to vary tremendously from place to place and provider to provider, and so it's going to still be confusing, but I guess we are stuck with it, so we better absolve ourselves to it. It will begin by what's going to happen with the most recent IARC meeting, where there's going to be processed meats, which are considering to be causal, if I understand correctly, but the book hasn't come out yet. And if that's true, then we are going to have another listing from an authoritative body on the

food stuff.

COMMITTEE MEMBER REYNOLDS: But that's not a chemical --

ACTING DIRECTOR ZEISE: And Carol Monahan Cummings, I don't know if you want to clarify around that, Carol. Our chief counsel.

CHAIRPERSON MACK: Anyway, so I guess we'll -- let's take Shanaz's suggestion for five chemicals. And let me first ask our director here, do we need to come into complete agreement on what to do, or can we just list some things for the staff to think about -- about further listing?

ACTING DIRECTOR ZEISE: That will work fine.

CHAIRPERSON MACK: Okay, so --

ACTING DIRECTOR ZEISE: And so we would -- if you could discuss it, and it would be great if you could give us some direction, but if you'd like us to bring some subgroups back to you for consideration, I think just getting a general direction will be good, and we can always follow up.

CHAIRPERSON MACK: Okay. I personally don't have any suggestions. I think it's a tough deal, and I think we are going to wind up with foods, but from what David said -- what Shanaz said, we might have some ideas. So let's just go through and ask one by one.

COMMITTEE MEMBER EASTMOND: Well, the only thing that's, in my mind, if you are looking at classifications that might be worth pursuing are small molecular weight ureas, because you had a series of them that were very positive, very strong. This is the ethylurea, methylurea, ethylene thiourea, and butylurea. And in those cases there appeared to be a clear interaction between the urea and the nitrite and very strong responses.

The question is, are there others -- can you exclude others that aren't -- wouldn't fall within that category, and that's something that I think look at to see if it's worth pursuing. And I would leave this, really, at OEHHA's good judgment to say is this worth pursuing or not. Jason, some thoughts?

COMMITTEE MEMBER BUSH: Same thoughts. The -- you know, the ureas jumped out as strong positivity for tumor findings. I think trying to get a handle on some other subclasses, you really have your work cut out for you. You know, there's a suggestion of the carbamates, but, again, that's -- that may be difficult to assess that out a little bit. So as a first order, I think looking at the small molecule ureas are a place to start.

CHAIRPERSON MACK: Okay. Shanaz, why don't you

tell us your five chemicals.

COMMITTEE MEMBER DAIRKEE: Ureas were among them, but my understanding is ethylnitrosourea and methylnitrosourea at least are not relevant to humans, and these are specifically rodent carcinogens. This is my take on the literature, so I'm not sure if I'm that excited about those two, but I was very intrigued that -- and, again, this may be true of the next two that I'm going to be mentioning, which is morpholine and aminopyrine. These two, I don't know whether there is any human data at all, but it was very intriguing to me that the animals work was strong and the genotoxicity work was very strong as well. It was a very good match. So data wise, those are the two that really shine as next things to be pursuing. Again, as I said, I don't know what the human data statuses are, but they are very widespread. They are common chemicals.

CHAIRPERSON MACK: Joe, do you have any suggestions?

COMMITTEE MEMBER LANDOLPH: Yeah, I would -- I would focus those which seem to have some human exposure and human problems, and among those, the ones which have the strongest animal carcinogenicity and genotoxicity data. There are also some drugs in there, which I thought were interesting. I was speed-reading last

night. Praziquantel and drugs likes this. So I think that could be a real problem for the public if they could be nitrosated, and so if they have strong evidence behind them, then I would bring them forward too.

CHAIRPERSON MACK: Peggy?

COMMITTEE MEMBER REYNOLDS: No. I defer to the table.

CHAIRPERSON MACK: All right. Now finished with the listing of process, so we'll take our lunch break under the --

CHIEF COUNSEL MONAHAN CUMMINGS: No mic. Can you turn the mic on?

ACTING DIRECTOR ZEISE: You just asked -- Dr. Mack just asked when you come back, so about a -- you think an hour is sufficient for the panel?

CHAIRPERSON MACK: It's sufficient.

ACTING DIRECTOR ZEISE: Okay. So come back at 1:00.

CHAIRPERSON MACK: Come back at 1:00.

ACTING DIRECTOR ZEISE: 1:00?

CHAIRPERSON MACK: 1:15.

ACTING DIRECTOR ZEISE: 1:15.

(Lunch recess was taken.)

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DR. SANDY: So the item now that we are going to

discuss is prioritization of chemicals for CIC review. And many of you have joined the Committee since the last time we brought a group of chemicals for prioritization ranking in 2011, so I'm going to give a little bit of an overview of what this process is that we call prioritization.

So we track chemicals that we think have some evidence of carcinogenicity, and we then prioritize among this large group of chemicals. And the goal is to identify chemicals that you, the CIC, should evaluate. And we want to focus your efforts on chemicals that may pose significant hazards to Californians, so we look at chemicals that we think have apparent exposure in California, and then we look at chemicals with the most information that suggest they might be carcinogenic.

I want to emphasis that prioritization is a preliminary appraisal of the evidence of hazard. It's not a thorough comprehensive review like we do when write a Hazard Identification Document. It's meant to be a quick screen.

So here's a schematic from our prioritization process document. We have this tracking data base, and then among the chemicals that have evidence of apparent exposure in California and some carcinogenicity evidence, something suggestive of carcinogenicity, we

come up with a group chemicals call the candidate chemicals, which are flagged here. And we apply different data screens to those candidate chemicals, where we do focused literature reviews to identify chemicals that we should take further into the process. And we've met with your committee over the years, and you've instructed us to -- that you are most interested in chemicals that have evidence in humans, so we apply a data screen -- a human data screen, and then we also apply an animal data screen. We have done this in the past. And then we come up with chemicals that we want to propose to you for consideration, and we consult with you in a meeting like we are doing today. And then we take your advice and we -- OEHHA then selects chemicals for preparation of hazard identification materials.

So in 2009 through 2011 we were applying human data screening and an animal data screen to about 380 chemicals, and we screened them. And chemicals that passed either one of those data screens, we then looked at in more detail. And the ones we thought were the most compelling, we brought to you. So we brought 104 of those chemicals to you for ranking during those three years. And now we are doing ongoing screening as we add new chemicals to the tracking database, we screen immediately to see if there's apparent exposure in

California, and we look at the evidence and we come up with an assessment of our own. And if we think that we need to take it to you for consultation, it goes on our list to do so.

We also update the chemicals we screened back in 2009 to 2011 looking for new information in the scientific literature. And so we have ongoing proposals of chemicals for the CIC's consideration, and we consult with you on an ongoing basis. So here we are today consulting with you on five.

Here's another screen, just of our process. We apply a human data screen, we apply an animal data screen. Anything that passes either one of those, we then do step three, which is we conduct a preliminary toxicological evaluation of that chemical, and that means we look at all relevant data -- animal, human, mechanistic data, and come to some assessment of what is the strength of that data. And the ones that are the strongest, we identify as chemicals we want to propose to you for consideration, step four.

The human data screens, is -- is here. We look at epidemiology studies that report positive associations between exposure and increased cancer risk. We give more weight to analytical studies and to the studies where the cancer effect can be attributed to the

chemical with some confidence.

The animal data screen is laid out here. Again, this is a just a quick way to pull out chemicals with what we thought were the strongest levels of evidence, and we've consulted with you on this screen as well. So if a chemical has two or more positive animal cancer bioassays or one positive study with malignant tumors or combined malignant and benign tumors occurring to an unusual degree with regards of incidents, site, or type of tumor or age at onset; or if we have findings of tumors at multiple sites or evidence of a second animal study of benign tumors known to progress to malignancy, then we say the chemical passed the animal data screen.

So this slide shows where we are today in our prioritization process for consulting with you on five chemicals, and here they are. Your committee in the past has asked us to put a table together like this, where we try to characterize the exposure to each of the chemicals as either being wide spread or high in frequent consumers or limited exposure, perhaps occupational, or high in infrequent consumers, so we characterize exposure. And then for the different types of data -- human data, animal data, and other relevant data, we are indicating with an X that there are studies to look at. An X in the analytical human data column

does not mean it's positive analytical data. It means there's a study. And the idea was to guide the epidemiologists and toxicologists and other scientists as to what they might want to focus on in reviewing the prioritization materials we give to you.

So the five chemicals we'll be discussing today are aspartame and then asphalt and asphalt emissions associated with road paving. We are also asking you to look as asphalt and asphalt emissions associated with roofing. And then we have methyl chloride. The next one is a group of chemicals, type-I pyrethroids, and as I've indicated here, two of the pyrethroids have been ranked by your committee in the past -- permethrin and metofluthrin -- but we are bringing the group, and you have the ability to rank the group or individual chemicals within and group, and then vinyl acetate. And I've also noted for aspartame that it was ranked by your committee in 2009, but since that time, there's new evidence. That concludes my presentation.

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CHAIRPERSON MACK: Okay. We'll begin with aspartame. And Dr. Eastmond and I are designated to provide our opinions first, so I'm going to ask Dr. Eastmond to tell me what he thinks.

COMMITTEE MEMBER EASTMOND: I'll kind of give

you my overall assessment and aspartame story. Basically, there's a significant association between aspartame and Non-Hodgkin's Lymphoma was seen in males in one prospective cohort study. In a second study, although significant increases were seen at lower doses, the increases were not seen at higher does, and there was no significant trend related increase, and the third prospective cohort study showed no association with Non-Hodgkin Lymphoma.

The animal studies, this is one there's been a lot of work done in animals, certainly rodents, and what you see is sort of mixed in inconsistent results on those animal bioassays, so -- I'll just go through it. Negative results were seen in male and female mice reported in one study. Increased in liver tumors were seen in a transplacental plus lifetime exposure in male, but not female mice, and there was a possible increase in brain tumors was also seen in rats. Another plants -- transplacental plus two years study in rats showed no treatment-related findings. Another study in rats showed no treatment-related increases. Two lifetime studies in rats conducted by the Ramazzini Institute report increase in leukemia and lymphomas. Increase in kidney tumors was also seen in one of the studies and increased in mammary carcinoma in males and

females in the other study.

The kind of -- a little bit unusual. The leukemia lymphoma results from the Ramazzini Institute during that period of time are not considered to be reliable because they had problems with an infection, and there were some issues with the pathology diagnosis. So I believe that during this period of time, the solid tumors results are considered to be fairly reliable, but those on the leukemias and lymphomas are considered questionable.

As far as genotoxicity, there's been positive results reported on a number of genotoxicity tests; however, from my point of view, the quality of these results is suspect, partly because they've been published in journals where I can think the editors and the reviewers are unlikely to have much experience with these type of assays, so I look at this sort of medium priority. Be high because of exposure and concern about it, but the data that I can see itself puts me a little bit lower, so that's my assessment

CHAIRPERSON MACK: Well, with respect to the epidemiologic studies, I think there's always reasons for caution and interpretation, but the fact is, that Non-Hodgkin's Lymphoma's popped up twice. Whether or not those were serious findings or not, we don't know.

I think one of the things that weighs on my assessment is the fact that this is an extremely widespread agent, and kids are drinking it every day. And, furthermore, if we decrease the sugar -- sugary drinks that we'd like to decrease in the country, that means there's going to be more consumption of aspartame, and, therefore, I think it's more important on that basis. And I'd like to add that it's also a commercially really big deal because it's -- involves an awful lot of sales and awful lot of business activity, and to me, that doesn't mean it should be downgraded; it means it should be upgraded, because a decision should be made as soon as possible and based on the evidence as to whether or not we are having any concerns. If it turns out that the epidemiologic data is faulty and there is no additional animal data or genotoxicity data, that means we can dispense with it quickly and go on to other things. So my inclination is to call it high, even though I respect David's strictly scientific view that it might belong in the middle.

COMMITTEE MEMBER BUSH: Yeah, after reviewing the available data, I mean, there is so much out there, I -- my conclusion was to put it somewhere in the middle in terms of a priority listing.

COMMITTEE MEMBER DAIRKEE: I would say middle to

high. Middle to high.

COMMITTEE MEMBER REYNOLDS: Middle to high.

CHAIRPERSON MACK: Middle to high is not a category.

COMMITTEE MEMBER REYNOLDS: Okay. High.

CHAIRPERSON MACK: Okay. Shall we take a vote? Pick comment. Let's now have some information from other people.

CHIEF COUNSEL MONAHAN CUMMINGS: Your mic is not on.

CHAIRPERSON MACK: Let's go now to the community, and let's start with the folks from Georgia, so Ms. Martini, you want to -- and please strictly stick to five minutes. Yeah, it's too many books for five minutes.

---oOo---

MS. MARTINI: First, I want to thank the Committee because this is such an important -- this is such an important subject. It is very much appreciated. In fact, as I walked in, I was met by a very charming man from Romania, and he reminded me that Romania is the first country in the world to ban aspartame six years ago because it caused so much cancer. And what I was going to say is a little bit different than what I'd like to say now because you mentioned the Ramazzini

studies. And I was that Dr. Soffritti in New York when he got an award for how prestigious they were, and I worked with EFSA and I see it back there in your book. And here's what happened is, Dr. Cola, who headed EFSA resigned because industry tried to get them to say that the Ramazzini studies were not -- were not good. And they came up -- they said, the rats have respiratory disease. Well, Dr. Soffritti said, of course they do; it's a lifetime study. And respiratory disease is the dying process, and the rats were dying.

Now, there have been three Soffritti studies or Ramazzini studies, and it showed it to be a multipotential carcinogen. And then Harvard did a study on it, which was a human study, they said was the longest and strongest to a link for cancer. But, first of all, knowing that I couldn't speak very big, I brought the medical text to show it to the Committee, and it was cut down 40 percent and had everything as a matter of public record to help you with being brief.

I've provided you with a sheet that I copied from this on the mechanisms by which it causes cancer. Now, this is, for instance, Dr. Roberts, who was the world expert, says that diketopiperazine, derivative of aspartame has been incriminated as a tumor-causing chemical. It caused brain tumors in original studies,

and the Jerome Bressler to the FDA is the one who wrote the Bressler report that's on my website, MPWHI.com.

And when he retired, I called and thanked him for this report, and he says, "Didn't you notice something was missing?" And I said yes. I didn't know what it was. He said, "You've got to get those two studies, because people are using this stuff, and it's -- and it's deadly."

But it took me eight years to find those studies that I've added back to the Bressler report. They were teratology studies, and they showed neuro tube defects. And the FDA made a deal with G.D. Searle never to let the public know. And what's happening, there's no pregnancy warning, and so the -- they're using aspartame and they're giving birth to babies with brain tumors. St. Jude is full of them. When I gave these studies to Dr. Monte, and he wrote a book about it, While Science Sleeps, the Sweetener Kills. And in the last chapter, you can go to While Science Sleeps on aspartame and autism, and he explains how they blew up his house because he was telling all this stuff -- with him in it, I might add, and then the fact that the FDA made a deal. But once I exposed it and put him back on the Bressler report, then the FDA released another one. He'd been trying to get it for 30 years, and Dr. Monte wrote the

book. One victim was so upset about all the propaganda, that she did her own study. The tumors were -- and she wrote a book. The tumors were so large, the rats used them as pillows.

So then Dr. Peter Nunn in the UK did a study on brain tumors, and he knew Dr. Owney, who tried to prevent approval because of the brain tumors and the birth defects, and they never published it. I saw part of the beginning, and they told me, yes, it's like Dr. Owney found, so -- and it's so easy to prove. Incidentally, some years ago, the Winston Food Laboratory did an analysis on ten diet cokes that were in the fridge, ten in an incubator, ten that is -- that was at room temperature; and the Food Chemical News published that even the aspartame in the -- that was in the fridge had broken down to diketopiperazine.

And in closing --

CHAIRPERSON MACK: Thank you --

MS. MARTINI: -- the FDA admitted it was a carcinogen.

CHAIRPERSON MACK: Okay. Thank you very much. We appreciate your contribution.

MS. MARTINI: I've been doing it 26 years --

CHAIRPERSON MACK: I bet you have, and your style shows it.

Okay. Now we have Lisa Lefferts. Again, I'd appreciate you very much sticking to the five-minute deadline.

MS. LEFFERTS: Thanks very much for the opportunity to be here. My name is Lisa Lefferts. I'm a senior scientist with Center for Science in the Public Interest. We're an independent nonprofit organization concerned with public health advocacy. Oh, this is the wrong presentation, but I'll will work with it anyway.

Our bottom line conclusion is to urge the Committee to make aspartame a high priority. This would be consistent with IARC's recent decision to designate aspartame a high priority for review. As noted, it's one of the most widely consumed artificial sweeteners. We have positive findings in three animal studies, two species, both sexes, multiple sites, supportive human evidence. We do have a lot of negative studies, but those tend to be underpowered studies, and they do not provide convincing evidence of noncarcinogenicity. They don't outweigh the positive findings, and we urge the Committee not to rely on the EFSA review, which was flawed.

Exposure can be a lot higher than what was indicated in the OEHHA document. This is from the NIH-AARP diet and health study, which said that

consumption could be as high as 3400 milligrams per day, a lot higher than the approximately 200 milligrams per day equivalent mentioned in the OEHHA document.

The animal studies were published in peer review journals, two published in a government-sponsored journal, and they are far superior to the old industry studies because they are much larger, the animals were followed over their lifetimes, and two included in utero exposure.

There's a lot of rumors about the Ramazzini Institute, but the best information available on that laboratory can be obtained from the 2011 NTP EPA sponsored review, and they found that everything was within GLP expectations, slides -- all slides required were present, histological quality was very good. And there was also a review of chemicals that were evaluated by both NTP and the Ramazzini Institute, and it's, quote, found remarkably consistent results. These are the people that identified that benzene was carcinogenic first, and they were criticized then, and they are being criticized now.

This is a quote from the an article published by EPA scientists. They talk about aspects of a design including gestational exposure, lifespan observation, and larger numbers of animals in groups may in part

advantages that provide risk assessors with valuable insights for the identification of chemical-related neoplasia, not obtained from other bioassays, and that's exactly the situation we have here with aspartame.

We filed a Freedom of Information Act request. There was a pathology working group work report from NIEHS that was providing a second opinion on some of the diagnoses, and they found that the diagnoses of lymphatic and histiocytic neoplasms were generally confirmed.

In the 2011 review, which did not focus specifically on aspartame, there was wide spread agreement in diagnoses. The exception as was mentioned was the lymphomas, but the issue there was really a quantitative not a qualitative issue. There's three sets of data there. There's differing opinions on how many lymphomas, but they all did diagnose lymphomas, and EPA continues to use the solid tumor data.

I just want to draw the Committee's attention to the kidney tumors. There were none in concurrent controls, there've been none in the Ramazzini Institute controls historically, and they're almost never found in Sprague-Dawley rats historically, yet there were 21 out of 1500 treated -- Sprague-Dawley rats that had these tumors. And the experts that we consulted with who have

worked with NTP and IARC said these are considered clear evidence of carcinogenicity.

The argument that may be infection could explain the lymphomas and leukemias has been thoroughly evaluated and refuted by EPA scientists in the journals that I've mentioned here. The negative studies, the industry studies failed to meet the minimum number of animals per sex per dose, versus the RI studies, which greatly exceed those recommendations. The NTP transgenic studies are not considered reliable, and the limb study -- the exposures -- the subjects were late in life when aspartame was first approved.

Okay. That's all the time I have. The EFSA analysis is flawed, and that's our conclusion.

CHAIRPERSON MACK: Thank you.

MS. LEFFERTS: Thank you.

CHAIRPERSON MACK: Next let's ask Dick Adams.

MR. ADAMSON: Good afternoon. I'm Richard Adamson. I appreciate the opportunity to speak today. I'm here on behalf of the American Beverage Association and will share some information on the carcinogenicity of aspartame. I've been following aspartame since 1981 when I become director of the National Cancer Institute's division of cancer etiology, and I've kept the breast of the aspartame science for the past

35 years. The Ramazzini carcinogenicity studies have been brought up, so let me comment. They are seriously flawed. Board-certified pathologists, the national toxicology program, and many regulatory authorities have critiqued these studies extensively and repeatedly, and they report numerous problems in the design, conduct, and statistical evaluation of the animal bioassays.

The Ramazzini mouse study, which is our latest study, published by Soffritti et al is the latest study, and the European Food Safety Authority, EFSA, in 2011 dismissed this study and correctly noted, and I quote, It is generally accepted that lifetime studies until or close to the natural death can lead to erroneous conclusions, unquote, because of geriatric pathology and autolysis.

Also, in 2014, the Food and Drug Administration rejected a citizens' petition that asserted that the Ramazzini aspartame study showed carcinogenicity. The FDA, in reject it, noted they had asked for additional information and data from the Ramazzini Institute on all three studies and had not received any. Also worrisome is infection in the rat column, which you've heard about, with mycoplasma pulmonis, and the subsequent misdiagnosis of tumors.

The Ramazzini Institute does not use barrier

maintained specific pathogen-free animals in contrast, with those of the National Toxicology Program or other institutes. Schoeb and McConnell reported in a peer review journal that the Ramazzini rat bioassays were compromised by mycoplasma pulmonis infection, and lesions of the diseases were misdiagnosed as lymphoma. By the way, Schoeb is a leading authority on mycoplasma pulmonis in animals.

Also, it's been brought up about the EPA and EP pathology working group. Let me tell you what they said, and I quote, that tumor diagnosis and procedures at the respiratory tract and neoplasms of the inner ear, the diagnosis of lymphoma and leukemias are unable to be confirmed.

I do not believe that Ramazzini has allowed sufficient review of its mouse data to rule out the possibility of infection in the mouse colony. These are not barrier-maintained animals. Finally, no regulatory agency in the United States, Canada, Europe, Australia, or Asia has accepted the conclusions of the Ramazzini carcinogenicity studies on aspartame.

The currency I see priority level for aspartame, as you've heard, is at the bottom of the medium category, and I personally believe that is an appropriate level for aspartame today.

Thank you, and I'll be glad to answer any questions.

CHAIRPERSON MACK: Thank you, Dr. Adamson.

MR. MURRAY: Thank you. Jay Murray. On behalf the Calorie Control Council, thank you for reading our comments. We believe the data strongly support aspartame -- retaining aspartames at the bottom of the medium category priority level, which you assigned in 2009. The FDA in 2014 and the European Food Safety Authority in 2014 reviewed the carcinogenicity data concerning aspartame, including the most recent Ramazzini study, found no cause for concern and explained their reasoning in detailed reports available to the public. No regulatory agency in the world considers aspartame to be a carcinogen. The public comments you received express a lot of emotion mostly from outside of California, and with all due respect, it's not necessarily a public service, however, to dedicate your and OEHHA's future resources to allegations of government conspiracies. I got two slides. Thank you.

So the scientific data today is essentially the same as when you assigned aspartame to the bottom of the medium priority in 2009. There's only one additional animal study that was not considered by your committee

in 2009. That's the Soffritti et al mouse study. And as you heard from Dr. Adamson, studies conducted at the Ramazzini Institute have been the subject of serious criticism. This study is no exception. Both FDA and EFSA have not accepted the results of this study because of critical flaws.

Next slide. There are three epidemiology studies published since 2009 that were not considered by your committee. There's the Cabaniols case control study, negative case control study. The most recent prospective cohort study by McCullough et al in 2014. At the -- the -- and the Schernhammer study, which is a weak and inconsistent positive prospective cohort study where the authors did not rule out chance as an explanation, said that their results needed to be confirmed in other large prospective cohort studies, and even issued a press release stating the data is week. Importantly, no increased risk of cancer attributable to aspartame was identified in the other two cohort prospective cohort studies. So none of these studies warrant elevated aspartame's priority level.

Finally, an IARC advisory panel recommended that aspartame and sucralose be reviewed by IARC in the next few years, and this will mark the third authoritative body to evaluate aspartame. Both NTP and FDA have

concluded aspartame is not carcinogenic, and there's no reason to raise the priority level for a substance that's already been reviewed by two authoritative bodies and may be reviewed by the third.

In fact, the prioritization procedure states, quote, it's unlikely that chemicals will be proposed for CIC review that have been recently reviewed by an authoritative body and found to have insufficient evidence of carcinogenicity, yet we seem to have exactly that situation with FDA's 2014 review. FDA received two petitions asserting that aspartame is carcinogenic in animals, and under the Delaney clause, carcinogenic food additives are prohibited. After reviewing the assertion that aspartame was carcinogenic in animals and after specifically analyzing all three Soffritti studies, the FDA found no basis to conclude that aspartame causes cancer in animals or humans. This FDA conclusion was expressed in official FDA action dated October 2014 that rejected the two petitions. So according to the prioritization procedure, it seems to me that aspartame should be an unlikely candidate for CIC review. So for all of these reasons, aspartame's priority level should not be elevated, and I'd be please to address any questions you may have.

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CHAIRPERSON MACK: Thank you, Mr. Murray. And that concludes the conclusion on aspartame on the floor, so now let's see whether or not we have changes in our views.

Jason what do you think?

COMMITTEE MEMBER BUSH: I'll maintain my previous conclusion, and I believe it's at medium priority. And my rational for that was having the other authoritative bodies rereviewing this material.

CHAIRPERSON MACK: All right. David.

COMMITTEE MEMBER EASTMOND: I have sort of mixed feelings. I'm still in a medium sort of weight; although I can go a little higher, because the significance. There's obviously public concern about this, so I'm flexible about this. Yeah, I'm flexible about it.

COMMITTEE MEMBER DAIRKEE: Same, medium high.

CHAIRPERSON MACK: High or medium, but still medium. Joe.

COMMITTEE MEMBER LANDOLPH: High.

COMMITTEE MEMBER REYNOLDS: High.

CHAIRPERSON MACK: High. Okay. Well I found your arguments pretty good, actually, but I'm still going to stick with high, but I'd be happy with high medium, so we've got one, two -- they're still on four,

so it's going to be high. Let's say it's a low high.

Okay. That concludes the discussion of aspartame. Now, we come to the discussion of high and low asphalt --

PUBLIC MEMBER: Having trouble hearing you.

DR. SANDY: So I'm asking to put a slide up. You are talking about asphalt; is that correct?

CHAIRPERSON MACK: Yes.

DR. SANDY: Just to remind the Committee that we are asking you to rank two things, asphalt and asphalt emissions associated with road paving and assault emissions associated with roofing.

CHAIRPERSON MACK: So it's Peggy Reynolds --

COMMITTEE MEMBER REYNOLDS: To start with -- so they -- this is has been considered by NIOSH with health effects -- is there a reason for... is that an editorial comment that's going up?

NIOSH considered health effects in 2001, and as has been pointed out in some of the public commentary and the NIOSH report and the 2013 IARC report, in part, chemical exposures unlike aspartame, which may have very broad exposure for the general public. This is probably a series of exposures that are pretty much limited to occupational groups, specific occupational groups, and the nature of exposure may in fact be a function of

heating and mixing. The notation for NIOC -- IARC of excess lung cancer among roofers as opposed to among pavers may be a function of exposure to other agents such as cold tar or asbestos. So that is somewhat equivocal from the human health point of view. IARC similarly discussed issues about heating and the degree to which human exposures to some of these chemicals are associated also with exposure to cold tars, which are established human carcinogens.

The IARC multicenter study noted significantly elevated standardized mortality ratios for lung cancer for road paving workers, but not for roofers; although this study was based on very small numbers. And the IARC monograph cites several occupational mortality and case-control studies suggesting elevated lung cancer risks, but with considerable difficulties in interpretation, due to study design. And finally the 2015 meta-analysis of larynx cancer and occupations with PAH exposures suggested a nonsignificant elevated risks for asphalt workers. So from that perspective of the human health evidence, it does seem to have been addressed in a number of forums, and is -- the evidence is somewhat equivalent in my view.

CHAIRPERSON MACK: Peggy, equivalent is not a category.

COMMITTEE MEMBER REYNOLDS: Okay. We got high, medium, low; is that what we have? I would say based on the prevalence of exposure, importance to the general population, I would go low.

CHAIRPERSON MACK: All right. Dr. Landolph.

COMMITTEE MEMBER LANDOLPH: Yeah, it's an interesting group of substances to consider. There's a lot of polycyclic aromatic hydrocarbons in there. One of the studies indicates the higher the temperature at which it's prepared, the more carcinogenic activity it may have. So I agree with all Peggy's comments. I would rank it medium.

CHAIRPERSON MACK: All right. Howard Marks.

MR. MARKS: Thank you for the opportunity to speak on behalf of the stakeholders of paving asphalt emissions, and I'd like to -- my name is Howard Marks. I'm with National Asphalt Pavement Association. Also with me is Russell Snyder with the California Asphalt Pavement Association, as well as Paul Sohi with Asphalt Institute.

I do want to provide just a little background to the Committee here from my background. I've be practicing occupational health and toxicology for about 20 years now, have a masters in public health, and doctorate in environmental toxicology. I've also

published numerous articles on Ph carcinogenesis, an inhibition of that.

First off, I guess up on the board here, we have a distinction between asphalt emissions associated with road paving, which is the group I represent, and emissions associated with asphalt roofing. So someone had eluded to -- there's certainly a clear distinction in the chemistries of both paving asphalt and roofing asphalt, and especially in those emissions. I wasn't intending to elaborate much further on that. Much of that information is in our comments, and hopefully it you'll take some time to look at the comments and understand what those chemical differences are. A lot of it has to do with the application temperature.

Second, obviously, you've already talked about the occupational setting of exposure to these materials, not really public, and so it's extremely limited on the public. It is an occupational setting.

Third, there has really been no authoritative body, U.S. or international, that's really identified a carcinogenic hazard or risk for exposure to paving asphalts. Someone had indicated that -- about some of the epidemiological evidence, whereby there was misconstrued on relative risks with regard to paving and roofing, and hopefully you'll take another look at that.

But IARC itself had determined that there's no human evidence or animal evidence of carcinogenicity or cancers with exposure to paving asphalt.

Also, with regards to chemistry, there really is no study that's identified in field exposure emissions of paving asphalt fume. It has greater than three -- three rank PIHs, and that's because the paving temperature is usually below 300 degrees. We've also started to do some engineering controls on using paving applications machines that are basically reducing exposure to the workers as well as our industry has been proactively looking at new technologies to even reduce that a temperature further.

I guess the last thing I'd like to impress with the Committee is, basically, the reasons that are articulated in our written comments, and that is that there are significant differences in chemical composition between paving and roofing asphalts. These are primarily due to the application temperature. There's a complete lack of evidence for human or animal cancers or carcinogenic hazard or risk. And, again, the exposure is only under an occupational setting. So our stakeholders see no reason to really prioritize paving asphalt emissions, and we would respectfully request that that be removed from future listing. I can answer

any questions if you have any. Thank you.

CHAIRPERSON MACK: Thank you.

COMMITTEE MEMBER BUSH: I have a question. Thank you. Curious about the personal protective equipment that workers actually have. Never tend to see anybody wearing masks or filters or breathing apparatus in any way. Is that something that is being addressed or --

MR. MARKS: Thank you for mentioning that. There are two occupational exposure levels right now that are in place, one by Cal/OSHA and one by ACJH. They are very low and the emissions from paving occupational setting are well, well below those occupational exposure levels, so there's no need for PPE.

CHAIRPERSON MACK: You are referring to paving?

MR. MARKS: Correct. Thank you.

CHAIRPERSON MACK: Anthony Kriech.

MR. KRIECH: Thank you, Chairman Mack and the Committee, for taking a look at the documents we submitted, and hope you've had a chance to review them. My name is Anthony Kriech. I'm director of research or Heritage Research Group in Indianapolis, and for the last 27 years I've been studying asphalt and asphalt emissions. Today I'm presenting on behalf of AREC, the

Asphalt Roofing Environmental Council, which is a consortium of national associations related to the roofing industry. In order to understand a complex mixture like asphalt, the first thing you have to understand, it's not a single compound; it's lots and lots of compounds. And -- but for us to try to understand something complex like this, we decided early on to collaborate with the government -- NIOSH specifically -- with universities, and with the unions to try to understand what the exposures are to our workers.

The industry sponsored these collaborative studies in animal, mechanistic, and exposure measurements to get a more complete understanding of what is in the workplace that workers see each day. EPI has been challenging in roofing because of all the confounders. It's a smaller group. It's hard to get a lot of information around that.

When asphalt is at ambient temperatures, we know that asphalt contains low levels -- trace level of PACs, and those trace levels are well-established in the literature as -- and that is the concern that IARC has always had about asphalt emissions and exposure to asphalt. But when it is at ambient temperatures, the PACs that are present in the asphalt, the polynuclear

metacompounds are nonleachable by a number of studies in the literature, and there's really very little evidence that the solid asphalt itself is bioavailable. It's only when asphalt is heated up to high temperatures that any of these PAC compounds can be released. In fact, you need to get really above about 200 degrees C or 400 Fahrenheit for those compounds to get enough energy to get off the surface and form aerosols.

In order for those to get in then -- into the workplace environment, the breathing zone of workers, we have studied what conditions are necessary for that to occur. Roofing asphalt applications, which are heated above 200 degrees C, represent about 6 percent of all the roofing asphalts applied in California, and it's shrinking. And it's shrinking in part because of the published literature, which shows that when you heat these things up, you have a potential to release polynuclear aromatic compounds. So what we are seeing is a shift away from that.

Today, under the consent decree from the California Attorney Generals, roofing asphalt workers are warned about compounds that are known to cause cancer to -- in the State of California. So Prop 65 warnings are already in place for this industry. I was an observer at IARC in 2011 for the monograph 103 on

asphalt. IARC concluded that the concern in asphalt PACs, not some unknown compound that nobody knows about, the PACs that are well established, well studied.

They limit the conclusions to occupational exposure in roofers to a 2A classification, primarily based on animal studies, and those studies were actually, in part, sponsored by the industry, so I don't think there's a big controversy about that.

Hot asphalt applications above 200 degrees C is where we are concerned, and so we are trying to reduce those. So it's our opinion that the current Prop 65 warnings concerning roofing asphalt emissions are adequate today. Industry is moving to reduce temperatures further and to avoid exposures to these PACs. Our concern primary is that is listing the product from the standpoint of the cold material that's on the roof is a concern, because it will create confusion and not clarity around the concerns related to asphalt products.

I'm available to answer any questions.

CHAIRPERSON MACK: Thank you, Mr. Lee -- Kriech. Sorry. So now we go to the -- what the individual criteria -- what the individual classification should be. And I should have made it clear in the beginning, and I didn't, that we have to make two different

classifications, one for paving assault and one for roofing asphalt.

Jason, how do you think that falls out now?

COMMITTEE MEMBER BUSH: After reviewing the material, I -- looking at the totality of both the genotoxic data and the animal carcinogenicity studies, I'm -- I feel that it should be for both road paving asphalt and roofing asphalt, they should be listed with a medium priority.

CHAIRPERSON MACK: David.

COMMITTEE MEMBER EASTMOND: Similar opinion. I was thinking medium priority on both medium.

COMMITTEE MEMBER DAIRKEE: Medium. Medium for both.

COMMITTEE MEMBER LANDOLPH: Roofing medium, paving low.

COMMITTEE MEMBER REYNOLDS: Roofing medium, paving low.

CHAIRPERSON MACK: And I think what's I think too, roofing medium and paving low. And so let's go through with one, two, three, four for that, and so that's what's going to prevail. So it's going to be roofing medium, and paving low.

CHIEF COUNSEL MONAHAN CUMMINGS: Mic.

CHAIRPERSON MACK: Now Shanaz for methyl

chloride. Shanaz.

COMMITTEE MEMBER DAIRKEE: So for methyl chloride, it's important to note that the contribution of this chemical from natural sources is estimated to be as much as 99 percent of the total released. And thousands of tons of methyl chloride are released naturally into the atmosphere every day by volatilization from the oceanic reservoir, from volcanos, from forests and brush fires. And this chemical, because it's so ubiquitous, it is detected in drinking water, groundwater, surface water, seawater, all kind of effluent sediments in the atmosphere, in fish samples, and in human milk.

The few studies that have examined the carcinogenic potential of methyl chloride in humans through epidemiology have failed to demonstrate any association. And in animals, the only evidence of carcinogenicity comes from a single two-year bioassay in which statistically significant increased incidence of renal benign and malignant tumors was observed in male, only male B6C3F1 mice, but at very high concentrations. And it's also thought that the underlying mechanism of renal carcinogenesis in mice is not relevant to humans. It is genotoxic in a variety of test models, but at relatively high concentrations.

So it seems like the natural background of methyl chloride is pretty high, and to see anything above that from this synthetic or industrial sources requires very high concentrations. It is a group 3 chemical on the IARC list, not classifiable as a carcinogen since there is currently in adequate evidence for the carcinogenicity of this chemical in humans or animals. So I would tend to put it low on the category.

CHAIRPERSON MACK: Okay. Well, I was impressed by this one Icelandic study, which I don't know the detail's about, but a very high relative risk, and a significant one, of a 9.35 after 40 years of follow-up with fishermen that were accidentally exposed to methyl chloride as a refrigerant. So on that basis, I would tend not to want to put it low, but because of the rest of the data, I think I would probably go with medium. And since we have no other information available, let's now just go to see what other people --

COMMITTEE MEMBER BUSH: My opinion was to list it as medium priority.

COMMITTEE MEMBER EASTMOND: Mine is also medium, medium low.

CHAIRPERSON MACK: Okay. And Shanaz is at low?

COMMITTEE MEMBER DAIRKEE: I said low.

CHAIRPERSON MACK: And Joe?

COMMITTEE MEMBER LANDOLPH: Medium.

COMMITTEE MEMBER REYNOLDS: Medium medium.

CHAIRPERSON MACK: So medium prevails for methyl chloride.

Okay. Now we come to a really important issue, the pyrethroids, and important for no other reason -- if for no other reason because it's one of the ways we get rid of aedes aegypti and prevent zika and yellow fever and whatever else happens. So we need to try to be careful. David, you're the leadoff person for that.

COMMITTEE MEMBER EASTMOND: The -- so this is really a class of chemicals. It's type-I pyrethroid. So there are eight specific different chemicals that were listed in going through this. So, essentially, my take on epidemiological studies, there were multiple associations reported, particularly for exposure in utero and childhood leukemia. However, most of those with very strong associations appeared to be from one Brazilian study, so I didn't know what to think about that. And the animal bioassays, there were mixed results seen for the different pyrethroids somewhat inconsistent. You have -- depending on the particular agent, you'll have different tumor types, but there's a smattering of different tumors for the various types. So typically you'll get maybe increases in mice and a

couple of target tissues, but nothing in rats and negative in genotoxicity assays for pyrethrin, would be an example. So you've got this sort of mixed pattern going through this. I think Martha mentioned a couple of these already listed, if I'm not mistaken.

DR. SANDY: One is listed, resmethrin, and two have been brought to you separately for prioritization ranking.

COMMITTEE MEMBER EASTMOND: Okay. So which one is the first thing I'm listing?

DR. SANDY: Resmethrin --

COMMITTEE MEMBER EASTMOND: Resmethrin --

DR. SANDY -- is listed --

COMMITTEE MEMBER EASTMOND: -- is listed --

DR. SANDY: -- currently --

COMMITTEE MEMBER EASTMOND: Okay.

DR. SANDY: -- as a carcinogen. And then permethrin was ranked as a medium, I believe, and metofluthrin as a low.

COMMITTEE MEMBER EASTMOND: So there's a -- I mean, my take on this is that there are a variety of sort of reports for increasing tumors. I don't see any real consistency, you know, if you are looking at they all cause liver cancer or they all cause -- so it's a mixed bag. I don't feel confident in certainly treating

them as a class by themselves. I think we can go through individually on specific ones if we felt like it was warranted. And, again, you see these are typically sort of negative in genotox assays, although there is some positives, so it's a mixed bag. And so my overall kind of assessment on this, if I recall, was I put these down as sort of medium priority for full evaluation.

CHAIRPERSON MACK: I actually felt the same way, but my first thought is these should be dealt with individually, including the ones that have already been listed, so that we should consider looking at each of them -- I think there's seven -- each of the five remaining pyrethroids individually. And there doesn't seem to be consistency within each one, from what we know, so I would consider them either low or medium, and I guess I would go with medium also.

So now let's hear from Stan Landfair.

MR. LANDFAIR: Hello, Dr. Mack, Dr. Eastmond, Dr. Zeise, and panel members. Thank you. Thank you for reviewing our materials. I can tell from the preliminary comments you reviewed them carefully. We thank you for that.

I'd like a point of clarification. We understand from the notice there are two separate questions raised. One is whether the type-I pyrethroids

should be considered for listing as a class; and the second is whether, if so, they should be assigned a high, medium, or low priority. And I suppose we have a tertiary question as to each of these chemicals, what priority they might be assigned. And our -- I'd like to introduce myself. I represent Bayer Chemical Company -- I'm sorry -- Bayer Agri Sciences. And my colleague Arthur Lawyer, and Dr. Arthur Lawyer represents them also. We also represent Sumitomo. So of the eight chemicals listed, we identify with four, and so we will speak to those generally. There are also others behind us who will speak on behalf of FMC with respect to bifenthrin, and also from the Consumers Specialty Products Association, Dr. John Ross, who will speak with respect to the idea of whether these pesticides should be -- yes, these pesticidal chemicals should be treated as a class, although if that question is moot, then we probably won't need to address it.

So our position is that the chemicals should not be treated as a class, largely for the reason you mentioned, Dr. Eastmond. And really extension of the same discussion we had with respect to -- what chemical were you talking about earlier? It was nitrites. Nitrites. Your analysis. And that there are many chemicals that -- there are here eight identified, but

the are many more potentially type-I pyrethroid chemicals, and they don't show any kind of consistency in a mode of action or even in results for animal bioassays, so it would be wrong to assume that they should be treated as a class. And we think you've implicitly made that decision already by joining them.

You have indicated preliminarily that you thought these should be medium or low. I'd like to persuade you, they should be low, and part for the reason you eluded to with respect to their -- the compelling need for these chemicals in the mosquito and vector control. One of the criteria in your criteria is exposure. We'd acknowledge there is human exposure, but let's put an adjective in front of that word "exposure." The exposures here are regulated, they are low, they are deliberate, and they are for a public health purpose. These chemicals have been reviewed, all of them, in the United States by the U.S. EPA; by California's DPR; and other countries by agencies such as the Canadian pest -- the MRA, the pesticide regulatory and management agency; similar agencies in Europe; the World Health Organization.

We don't have to have an imminent concern that unless OEHHA or you, on behalf of Prop 65, step in and identify these chemicals as carcinogens, there will be

an unknown and unregulated danger. These chemicals are very, very well regulated, and that leads to the other questions, are they good candidates for listing? We think not. Remember, please, that U.S. EPA is an authoritative body, and if the -- and each one of these chemicals has been reviewed on the basis of a mountain of data for carcinogenicity. If the agency, this agency believed that those review demonstrated these should be listed, they would have been listed already in the authoritative bodies listing. That does not preclude your review, but we think it's very poor candidates for listings because of that.

Dr. Lawyer can address scientific questions regarding these chemicals, and so can the representatives of FMC and CSPA, if you'd like to hear more.

CHAIRPERSON MACK: Just to point out, though, while it's true, it doesn't preclude our review, it also doesn't excuse our nonreview. We are obligated by the State of California to do the job, whether or not somebody else has already done the job, so we have to make a decision.

MR. LANDFAIR: Well, I won't dispute that, but here, as you point out, we are talking about priority, and if the question is how should we devote the State's

resources, I think the need is far less compelling for pesticidal chemicals that are regulated and where the -- issue of carcinogenicity seems to be so attenuated.

CHAIRPERSON MACK: Right. I understand.

MR. LANDFAIR: Thank you.

CHAIRPERSON MACK: Next on the list is Arthur Lawyer.

MR. LAWYER: Artie Lawyer with Technology Sciences Group from Davis, California, also representing Sumitomo Chemical and Bayer Crop Protection, I think it is. I have two brief comments. One gets to the point that you were bringing up, Dr. Eastmond. This -- the class-I pyrethroids as considered as a group, it's quite a disparate group of chemicals. I mean, just as an example, the vapor pressure ranges over four orders of magnitude, the log P differs by over three orders of magnitude, so it's not surprising that in fact you would get a different toxicological profile for these chemicals. And as I think you've mentioned, the -- if you look at those compounds that actually do have potential for carcinogenicity and the -- and the classic studies that are done, some of them actually -- there's no consistency with what kinds of parameters come out. There's no target -- consistent target organ that -- rat versus mouse. Again, no consistency there. The male

versus female. So you look across the board. It's really an individual compound by compound matter. So that's point number one. And, in fact, to that point, resmethrin was brought up. It was listed, I think, eight years ago, and it had data for that particular compound that was consistent with listing under Proposition 65.

So the second and final point, is on -- on the fact that these are regulated compounds. All these pyrethroids are registered under FIFRA are by the EPA. And the good news about that is, as the summary document that was made available to you, they all have been looked at, and as -- in order to get registered in the United States, they actually have to go through a focused cancer assessment by the agency; so, in fact, all of these compounds, except those that have not been into the United States, have an EPA classification for cancer. And as you can see, resmethrin came up as likely, but most of them have popped up as not likely to be carcinogenic, so we have the -- an agency in many cases very recently coming to those conclusions, so it fits the criteria of how a regulatory agencies looked at it in the past.

For those that haven't been to the United States, I couldn't find any that haven't at least been

through the European agency, and, again, not found are the ones that were listed on -- before the Committee, none of them were found to be likely to be carcinogenic in the European way of looking at it. Again, so it gives you a preamble for how these compounds would likely be looked at by the Committee here.

So I was going to leave it at that, and see if there's any questions. We could go through individual compounds, but I'm not sure it's necessary.

CHAIRPERSON MACK: I have a question, and you'll probably think I'd ask, do they have all the same mode of action against mosquitos?

MR. LAWYER: No. There's actually two major mechanisms, but, largely, the answer is yes. I -- they target the neurological aspects of the insects, so part of that class difference has to do with that.

CHAIRPERSON MACK: Neurotoxicity is the same.

MR. LAWYER: Right. The target within the system is a little different, but in general, they behave much the same way, yeah. Very effective. Questions? Again, I could go through the individual ones.

CHAIRPERSON MACK: Okay. Tim Formella. All the way at the back. Takes you a minute to get up here, you know.

MR. FORMELLA: As introduction, I'm Tim Formella with FMC Corporation. I am in the regulatory group, so I don't have the science background that all of you folks do, but I just want to reiterate what has already been stated, that we don't believe that this group should be looked at as a group that each of the individual components of the type-I pyrethroids should be reviewed separately.

I -- when I look at this, I don't think you have captured each of the type-I pyrethroids. You have made a list of eight. I don't think that includes all type-I's, that may need to be looked at. And having said that, I don't know if you have had the opportunity to look at all the data that was listed for these eight. And if you are going to add all type-I pyrethroids, when you make this decision, that you probably need to review the data on all of those, so it may postpone some of those a little bit. So those are just my basic comments. And for bifenthrin, you can see by the data that's there, that I think that should be a low priority if in fact you do take the route of looking at them individually. Thank you.

CHAIRPERSON MACK: Thank you for your brevity, Mr. Formella.

DR. SANDY: Thank you. I wanted to just

clarify. We have suggested a group in this case, to allow you to give us advice on that group, possibly looking at that group, and we have listed some individual compounds within the group, but it's not an all-inclusive list, just to address this last speaker's comment.

CHAIRPERSON MACK: So you want an opinion on the group as well as what you should do in addition to that; is that what you are saying?

DR. SANDY: An opinion on the group and any individual compounds that you feel compelled to give us advice on that are not already listed. Thank you.

CHAIRPERSON MACK: Okay. Finally, we have Zhiwei Liu.

MR. LIU: So, first of all, thank you so much for having the opportunity. So I'm Zhiwei Lui, senior toxicologist, and on behalf of FMC Corporation. So I would speak specifically on bifenthrin. So basically, you know, bifenthrin toxicology document is complete, and it has been registered worldwide, include major agencies like EPA, AF, and European authorities. You know, for the U.S. EPA, so that currently the U.S. EPA doesn't have concerns about bifenthrin as a carcinogen with Q1 star. So, therefore, you know, there's no Q1 star approach for cancer risk assessment, so the cue to

reference those approach should be protect you of -- you know, any potential cancer concern. So, basically, I quote, the EPA said in their 2012 document bifenthrin is classified, you know, as a possible human carcinogen based on increased instance of urinary bladder tumors in mice, in the mice only, in the male mice only, single gender, in one single study. And -- however, the EPA concluded that bladder tumors may not be uncommon in mice are not likely to be malignant.

So, basically, all the, you know, tumor, basically -- you know -- basically, all the urinary bladder tumors in the male mice was reevaluated by the water pathologist group. They all included that urinary tumor, you know, cited in the original study report was actually, you know, the urinary bladder lesions. They are not tumors. As -- okay. In addition, this tumors were observed only in the male mice out of the highest dose tested, and in the instance, was over borderline significant. So, overall, I think all these tumors in the urinary bladder tumors are actually lesions not tumors; and, secondly, the only -- the basically the significant increase instance only of observed out of the high dose 600gpm, which is above the MTD dose. I think therefore, the recommendation of a note assigning Q1 star indicated that hemogenic potency of bifenthrin

is very minimal, and further demonstrated there's no major concerns for the, you know, carcinogenicity of bifenthrin. So, therefore, you know, we do consider bifenthrin should be set as a low priority for Prop 65. So with that, I would be happy to answer any questions.

CHAIRPERSON MACK: Thank you. I do have a question. I don't know who is the best person to answer it, and that is, when used in the field, as an insecticide class of pyrethroids, how much does it vary from place to place and from manufacturer to manufacturer in terms of the distribution of the individual pyrethroids? In other words, is it uniform mixed, or does the mix vary from place to place and manufacturer to manufacturer?

MR. LAWYER: Maybe I -- this is Artie Lawyer again. Maybe -- as part of the approval process by the EPA, if an agency says "thou shalt" and makes a label that restricts and makes very prescriptive how much material can be used and on what crops, it wouldn't exclude on some, allow on other. So, for example, you brought up zika. It's a very -- any of the mosquito uses, it's very well -- risk assessments, so it really depends on the crop, the use, and the potential for exposure, but it's part of the process.

CHAIRPERSON MACK: Thank you very much. Now, I

apologize to John -- I'm sorry. I got you out of order because I shuffled the cards.

DR. ROSS: No problem. I'm John Ross. I'm representing the Consumers Specialty Products Association, and I'm glad to hear that the Committee is considering not -- considering all of these members as a class, but rather individually, because a number of the compounds that haven't been considered don't produce tumors in either species that's been tested in either rats or mice. So things like permethrin, and imiprothrin, fenpropathrin, and others -- there's four or five of them, don't produce tumors in the species that have typically been tested, and so it would be a miscarriage to throw all these together.

Also want to reiterate that in animal testing, there is no single mode of action recognized with these. They produce tumors at different sites, and those produce tumors and in those chemicals where there has been extensive mode of action studies done, there is evidence that those tumors don't apply to humans. And one of the papers that you got in your file is for transfluthrin, which I helped write, addressing that issue.

I'd also like to go back to the question you asked about the amount used, and, for example,

transfluthrin may only need 2 milligrams in a room in order to repel mosquitos. It's extremely efficient because it's semivolatile. It's one of these compounds that is at the high end of the volatility range that Dr. Lawyer referred to, and that's compared with the chemicals that are used for treating West Nile by airplane. That maybe, you know, ounces per acre.

So to wrap up, there are no consistent activities in endocrine receptors. That's not a mode of action. And, finally, this epidemiologic study that's been referred to, the Ferreira study, I think is highly confounded because you have basically two socioeconomic groups that were examined. You've got a case-control study, but the cases and the controls come from entirely different economic groups, they're different skin colors, there's a variety of things. You've also got problems of translation going from Portuguese to English, and the biggest problem, I think, is recall bias. These individuals were queried months to years after their exposures.

With that, if you've got any questions, I'd be happy to answer them.

---oOo---

CHAIRPERSON MACK: Thank you. That's been very helpful, Mr. Ross. So a fifth question that might ask

is how you -- I keep turning it off -- how we would classify the pyrethroids as a group -- the type-I pyrethroids as a group for purposes of prioritization. So if we had to do it as a group, how would you classify it, Jason?

COMMITTEE MEMBER BUSH: Well, what struck me when I read the summary --

MR. LANDFAIR: May I intervene. I think the question on the notice was whether type-I pyrethroids should be treated as a class, and that's a threshold --

CHAIRPERSON MACK: --

CHIEF COUNSEL MONAHAN CUMMINGS: Dr. Mack, could you turn on your mic, please.

CHAIRPERSON MACK: -- that's been put to us, not deciding whether or not to do it.

MR. LANDFAIR: I understand that, and I'd accept whatever guidance my counterpart Carol Monahan Cummings says, but I understood the notice to put the question to the panel. They wanted your advice on whether or not type-I pyrethroids should be considered as a group or as a class; and, secondly, prioritization for the individual compounds.

CHAIRPERSON MACK: Yeah. I think we are getting to that.

MR. LANDFAIR: Okay.

CHAIRPERSON MACK: Thank you.

MR. LANDFAIR: Thank you.

COMMITTEE MEMBER BUSH: So what struck me when I read the summary is the -- the carcinogenicity, the animal data showing that there was some increases and -- of mixed -- mixed tumors, and not seeing anything related to the genotoxicity. You know, that stands out to me as a clear endocrine disruption. And the last gentleman that was just speaking, you indicated that there were no studies of endocrine disruption, but I -- in our summary, I see two, possibly three, different studies, and I'd like to know a little bit more. You know, it may not be that this -- this class of compounds or individual compounds are actually initiating tumors, but in my review of this information, it seems like they could be promoting tumors. And for that reason, one, I do not think they should be listed as a chemical group; and, two, I think they are of medium priority. I want to know more about these.

CHAIRPERSON MACK: If I understand you correctly, it seems reasonable to you to group them as a group rather than individually.

COMMITTEE MEMBER BUSH: No, individually.

CHAIRPERSON MACK: Okay. And medium -- if you had to list them as a group, you'd call it medium?

COMMITTEE MEMBER BUSH: Correct.

CHAIRPERSON MACK: David.

COMMITTEE MEMBER EASTMOND: As I said before and I think after the public comments made, that this is even a broader group than we've seen in our documentation, and so I think it would be -- I don't think it would be wise to take them all as a group, because they are highly varied, and there's many that apparently are not here and may not have any cancer data as well. If we chose to go forward and look at them, we'd probably ought to do this on an individual chemical-by-chemical basis.

CHAIRPERSON MACK: I -- I stay with my opinion that I voiced in the first place, that we probably should take them individually. I would also call them medium, if we had to do it as a group. But I would say, when I say we should do it individually, I don't think we need to -- I don't think it would be wise to try and cover every single type-I pyrethroid, because it's going to be a very large number and will take a lot of time, and there's very little data on some of them. So I think we have to, in some way, by staff or by us, but I think staff is the best way to make a list of those that we should cover individually. It will, of course, not include the ones that have already been listed, and will

include those in which there is some data that you've given to us already, and maybe we'll stop with that. That would be my personal opinion. But if I were to do it as a group, I would also call it medium. Shanaz.

COMMITTEE MEMBER DAIRKEE: I'm more inclined to look at them individually than as a group. Individually. Individually, as medium. Group, I'm not so sure.

CHAIRPERSON MACK: Let me ask you, if I understood you correctly, you are suggesting that each of them be considered individually --

COMMITTEE MEMBER DAIRKEE: Correct.

CHAIRPERSON MACK: Okay. I think that's hard to do without listening to data for each individual, but you have, and that's what you are deciding. Okay. Joe.

COMMITTEE MEMBER LANDOLPH: Yeah. A couple of interesting points. There is tumor genicity data in this memo out of the EPA I've got. It's interstitial cell adenomas of the testees, number one. Number two, I agree with Jason. There is data on endocrine disrupting chemicals. This is a paper from 2010 by Weis and Du et al, and they talk about members of this class acting by different mechanisms, but they have endocrine disrupting activities, which probably is why they don't have much genotoxicity. And number three, there's three

interesting papers, which deal with epidemiology data in increase in all lymphohematopoietic cancers and multiple myeloma in these three papers. So there's some epidemiology data too, so I would say take a look at them. I would say medium would be appropriate.

CHAIRPERSON MACK: Peggy.

COMMITTEE MEMBER REYNOLDS: So if I'm hearing the consensus is that we probably should not consider these as a group, but they are likely to be several members of a group that could be of importance, and we are deferring to staff to help enumerate those; is that correct?

CHAIRPERSON MACK: Seems we have somebody who is making a record of what we are all saying --

PUBLIC MEMBER: Having trouble hearing you.

CHAIRPERSON MACK: I say it's fortunate that somebody is making a record of everything we are taking, because it's so important, but as I understand it, we are agreed that we should try to group them individually or classify them individually.

COMITTEE MEMBER REYNOLDS: Right.

CHAIRPERSON MACK: We're also agreed that if we were forced to do it as a group, we'd call it medium.

COMMITTEE MEMBER REYNOLDS: Okay.

CHAIRPERSON MACK: And Shanaz, for one, is

prepared to call all of them medium on the basis of availability information, but we won't hold her to that.

COMITTEE MEMBER REYNOLDS: I agree with that, although I'm thinking we should address them as a group.

CHAIRPERSON MACK: Okay. Thank you very much.

COMMITTEE MEMBER BUSH: Dr. Mack, I have one question, actually to Dr. Sandy. Can I ask, is this type-Is pyrethroid being reviewed by the other committee, by the reproductive tox committee at all?

DR. SANDY: No, they are not.

COMMITTEE MEMBER BUSH: Okay.

DR. SANDY: If I could say a few more words. We were -- when we are asking you to group -- to rank the group, we might you -- if you ranked it as high, we might then use staff to figure out, which among those pyrethroids -- type-I pyrethroids as a group should be focused on in the Hazard Identification Document, like we done over the past few years with other groups of chemicals we've brought to you. We would not expect you to list the group. We would just bring them as a group to you, and you could list them individually. So I wanted to clarify that. But thank you for your ranking of this group. And then now, looking at the individual ones, if you saw any that you thought should be ranked differently than the whole group, we'd be interested to

hear.

CHAIRPERSON MACK: I'm going to ask the three non-epidemiologists for their opinions about that.

COMMITTEE MEMBER BUSH: At this time, I can't make a decision as to ranking individual compounds. I think if we are going to evaluate them -- and I know I'm not being very helpful to you; sorry, Martha -- I would need more time to evaluate the data.

COMMITTEE MEMBER EASTMOND: None of them jump out at me as being particularly more concerned than others. I mean, they are kind of this intermediate range for me.

CHAIRPERSON MACK: Shanaz -- or you've already expressed your opinion. Joe.

COMMITTEE MEMBER LANDOLPH: None.

CHAIRPERSON MACK: You don't think any of them stand out either; was that your answer? I'm looking for the person who wants to speak about vinyl acetate. So we'll go to vinyl acetate. Who's the -- Bush.

COMMITTEE MEMBER REYNOLDS: Okay. I'll start because there isn't very much epidemiologic evidence to refer to Dr. Bush. But IARC did classify vinyl acetate as possibly carcinogenic to humans through a group 2B, within inadequate evidence of the carcinogenicity in humans. Couple of the studies seem to be focused on

some cohort mortality studies, which were not necessarily geared looking specifically at vinyl acetate. One Union Carbide cohort mortality study looking at a number of suspect chemicals that suggested some elevated odds ratios for mortality for reticuloendothelial cancers, particularly Non-Hodgkin's Lymphoma, multiple myeloma, and lymphocytic leukemia, but based on extremely small numbers, nonsignificant associations, only two deaths to the -- for the lymphocytic leukemias. And then a study of a synthetic chemicals plant using a case control studies design; in other words, comparing lung cancers in the cohort compart to lung cancers in the community, to look at histologic subtypes, and finding some evidence for a higher proportion of large cell, but not other lung cancer histology as associated with vinyl acetate, potential vinyl acetate exposure. But this was again not statistically significant, and so it does appear that there is perhaps more opportunity than some of the compounds we've thought about for consumer exposures to the end products. I do not know enough about bioavailability for some of the end products, but would like to hear more about that.

COMMITTEE MEMBER BUSH: I did read the public comments from the -- from Franklin International and the

Vinyl Acetate Council, so thank you for providing that along with the 2008 risk assessment from the European Commission, all 257 pages of that, thank you, as well as the 2008 screening assessment from Environment Canada and Health Canada.

So the -- looking at the data, I'm going to focus on the animal carcinogenicity data and the genotoxicity data. The studies primarily indicate in animal studies that long-term exposure, either through drinking or inhalation, lead to tumor types of those particular cavities, so it's consistent with direct exposure. So we are getting thing likes increases in oral cavity cancer, esophageal cancers in the drinking studies, getting things like nasal papillomas in the nasal cavity, the tumors in the inhalation studies. So those do come from primarily high dose studies as well, so those need to be taken with a -- with an objective eye. There is overwhelming genotoxicity data. I think it's overwhelmingly positive, and it's consistent with the general mode of action of acetaldehyde being a primary metabolic metabolite of vinyl acetate. I realize in reading the public comments that there are exposure limits, and it doesn't seem as if the general consumer or -- would be in any danger of exceeding any kind of exposure limit there, and I think the

genotoxicity data is consistent, again, with, acetaldehyde being the primary genotoxic metabolite for this compound.

So I think the high dose animal carcinogenicity studies, you know, suggest this direct exposure, and in a real-world scenario, probably wouldn't be something that would be that much of a concern, I suppose, to the general public in California, and so I rank this as a low priority.

CHAIRPERSON MACK: Okay. Jason says low priority. Peggy, I didn't get what you said. High, medium, or low?

COMMITTEE MEMBER REYNOLDS: I was going to go medium, but I would like to hear a little bit more.

CHAIRPERSON MACK: Yes, there he is.

CHIEF COUNSEL MONAHAN CUMMINGS: We've already been going for two hours. I think that we should take a break soon for the court reporter. Yeah, two hours is long time for a court reporter.

(Brief recess was taken.)

CHAIRPERSON MACK: Okay Mr. Valentine.

MR. VALENTINE: Thank you very much. Can you hear me? Mr. Chairman, ladies and gentlemen of the panel, my name is Rudy Valentine. I'm here representing the Vinyl Acetate Council. I'm a board-certified

toxicologist, and the VAC, the Vinyl Acetate Council is a not-for-profit organization representing the major manufacturers of vinyl acetate.

You've already received our written comments of some of the concerns expressed about the mode of action in this material were pertinent to the discussion. I hope to enumerate some of those. My presence here, in bottom line, is to request that the CIC place low priority on vinyl acetate based on its mode of action as well as the very low potential for exposure to vinyl acetate in products that are used within California.

Vinyl acetate is a volatile ester. It's volatile ester, and it's mode of action, as already noted, is driven by the active metabolite acetaldehyde, which is formed from endogenous carboxylesterases, which is present along the portals of entry for which vinyl acetate may be exposed -- inhalation, nasal cavity, and oral cavity by ingestion. Complete metabolism of vinyl acetate also results in the production of an acetic acid, which can increase intercellular acidity and induces cytotoxicity. These play a role in vinyl acetate's mode of action.

Acetaldehyde notably is -- or can form DNA attics. It's weakly genotoxic, and of importance to the CIC, it's ubiquitous in the environment. It's present

and ambient there, and it's endogenous in most animal and plant life, included in many foods and fruit juices. It should also be recognized that acetaldehyde is approved of a food-flavoring agent, and is generally recognized as safe by the FDA. And while it is true, we acknowledge that vinyl acetate has produced tumors in some but not all species of animals. It has produced tumors by inhalation or oral routes. It's also important to recognize that tumors occur all along the portal entries and is not seen systemically. Further, tumors are seen only at very high exposure concentrations that are typically associated with either local cytotoxicity or increase cell proliferation.

OEHHA's toxicology summary that was presented to the CIC excluded the extensive mechanistic toxicology data that supports the view that acetaldehyde toxicity is dependent upon on acetaldehyde, and that both substances can be threshold carcinogens; that is, there's a biological threshold below which there should be no reasonable risk of adverse effects. This view has been endorsed by scientific experts. You've already alluded to the European review in 2000 as well as the Health CANADA assessments, and they concluded -- and I want to quote this -- the genotoxicity data are in line with the hypothesis that vinyl acetate genotoxicity is

mediated by acetaldehyde and that the genotoxicity of acetaldehyde only becomes evident after the cellular defense mechanisms are overloaded.

Further, the VAC contends that the available health and exposure information worked the designation of vinyl acetate as a low priority for review. In assessing prioritization, the VAC asks the CIC to consider whether a potential listing of vinyl acetate would in fact likely result in an issuance of any warnings. In the VAC's written comments, we noted that exposure to vinyl acetate from use of consumer and professional products are sufficiently low, such that it isn't likely that businesses would need to warn if vinyl acetate were ultimately listed. The VAC maintains that the projected internal dose and asks that risks associated with acetaldehyde from either inhalation or ingestion of vinyl acetate from consumer products is de minimus when compared to existing exposures from air, food, or as a breakdown product from ethanol consumption in beer, wine, and other beverages. And as part of that basis, we wish to note that, again, there was Health Canada assessment. During that assessment in 2008, industry provided a voluminous exposure information on consumer products. And what they observed after analytical measurement of most consumer products is that

residual VAM, which is residual monomer in materials that with made from vinyl acetate based polymers are undetectable. In the few cases where vinyl acetate was in fact detected, the concentrations were low, typically 300 part per million, or less.

While we maintain that there's sufficient justification for a threshold mode of action for VAM to assess the CIC, consider whether to designate VAM as a priority substance, we developed health benchmarks following OEHHA's default linear multistage methodology with a ten to the minus fibrous for cancer. Bottom line is all of those exposures are, at least in the order of magnitude, below a threshold of concern for vinyl acetate. I'll be glad to answer any questions.

CHAIRPERSON MACK: Okay. Let's recap again. Jason, where is your categorization?

COMMITTEE MEMBER BUSH: Low priority for vinyl acetate.

CHAIRPERSON MACK: David.

COMMITTEE MEMBER EASTMOND: I actually gave this a higher priority simply because there's a lot of consistency in the animal bioassays in the same types of tumors types were showing up in rather -- basically, within the site of exposure. I do recognize that for comments, apparently, there's been a lot of work

mechanistically that suggests this is a high-dose phenomenon, but that can be worked out at a later date, that sort of the risk assessment part of this process.

CHAIRPERSON MACK: You are calling it medium?

COMMITTEE MEMBER EASTMOND: I was going with high.

CHAIRPERSON MACK: You're calling it high.

COMMITTEE MEMBER EASTMOND: Or medium high, but I'm at high.

CHAIRPERSON MACK: Okay. I was coming down at medium.

COMMITTEE MEMBER DAIRKEE: Low.

COMMITTEE MEMBER LANDOLPH: Medium. Lots of genotoxicities.

COMMITTEE MEMBER REYNOLDS: Medium.

CHAIRPERSON MACK: Medium, medium, low, medium, high, low. So we have three mediums, a low, and high.

PUBLIC MEMBER: Microphone.

CHAIRPERSON MACK: We have three mediums, a low, and a high -- four mediums, a low, and a high. So it's going to be medium.

Finished with the prioritization. And Gary Roberts would like to make a brief but very pertinent comment, no doubt, on prioritization itself.

MR. ROBERTS: I have a question. Dr. Dairkee,

we were trying to make sure our notes reflected what you said about your views on the priority of aspartame. Our notes had that your view was medium with a note that it was high within the medium group; did we -- are our notes correct?

COMMITTEE MEMBER DAIRKEE: Yes.

MR. ROBERTS: Thank you.

The question was necessary because not everyone was speaking into the mic during certain parts of the meeting.

CHAIRPERSON MACK: No doubt. I'm not -- in any way doubt that. Anybody else have any questions? We have some history here? Carol have anything to say? You have an update of the section 27000 list.

CHIEF COUNSEL MONAHAN CUMMINGS: Okay.

CHAIRPERSON MACK: All right. Do I read this?

CHIEF COUNSEL MONAHAN CUMMINGS: Not yet

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CHIEF COUNSEL MONAHAN CUMMINGS: Let me give a little bit of background here. For this section of the meeting, as you may recall, the Prop 65 has two different lists of chemicals, one that you've been talking about a lot today that are chemicals known in the state to cause cancer or reproductive toxicity. The other lists that list are known as this 2700 list, and

it's a list of chemicals that need to have certain kinds of toxicity testing. And the way that we find out whether or not these chemicals should be on this list is we annually contact the U.S. EPA and the California Department of Pesticide Regulation and ask them whether or not they have any chemicals they want to add to this list that need to have certain kinds of testing done or where they have received the testing and the chemical might -- no longer needs to be on this list.

So what we wanted to do today is just go slide by slide, and that would be for this first -- for the first slide these are -- this is one chemical where the Department of Pesticide Regulation is recommending that we remove sodium fluoride from the list because they've received these two tests that were required to be done, and so this chemical no longer needs to be on this Section 2700 list.

So, Dr. Mack, if you'd be able to ask that question. Basically, what we are asking for -- we're just asking for your concurrence with what the information is that we received from these other agencies that --

CHAIRPERSON MACK: Okay. I'll read it. Based on the information that's been provided in the California Department of Pesticide Regulation, should

the chemical sodium fluoride, as identified on slide one, have endpoints removed from the list of chemicals required by the state or federal law to be tested or which have not be adequately tested as required? Would everybody who votes yes on this question, please raise your hand.

(Hands raised.)

CHIEF COUNSEL MONAHAN CUMMINGS: Is that five?

COMMITTEE MEMBER EASTMOND: If I can clarify, Carol. What you are saying is Department of Pesticide Regulation has informed you that they have received these tests, and so there's -- they don't think they should continue to be listed as being required because they currently have them?

CHIEF COUNSEL MONAHAN CUMMINGS: That's correct.

COMMITTEE MEMBER EASTMOND: Okay. So we are accepting that they have received these, and so we believe they are not needed?

CHIEF COUNSEL MONAHAN CUMMINGS: That's correct.

COMMITTEE MEMBER LANDOLPH: If my memory serves me right, the first carcinogenicity study on sodium fluoride was reported in an abstract from NIEHS, and it was positive. Whoever did the second one, wasn't too smart. They used different doses, which is the worst thing to do. So I don't think that first one, which was

positive, was ever replicated. In my mind it's not a settled issue.

CHIEF COUNSEL MONAHAN CUMMINGS: And just to clarify, this is not a question of whether or not these chemicals may or may not cause cancer. The question is whether or not the Department of Pesticide Regulation has received the testing that they had requested. So this list doesn't have anything to do with whether or not the chemical causes cancer. It's a list of chemicals where DPH or U.S. EPA has requested testing and has or hasn't received those tests. So DPH has told us that they received these two tests. They haven't necessarily evaluated them or made any determination based on that, but for this particular list, we just want you to concur with what DPR says in that they received these tests.

COMMITTEE MEMBER LANDOLPH: I don't see that I should have anything to say about that. If they say they received it --

CHIEF COUNSEL MONAHAN CUMMINGS: Well, I understand that but --

COMMITTEE MEMBER LANDOLPH: -- they received it. I'm not finished yet.

CHIEF COUNSEL MONAHAN CUMMINGS: Okay.

COMMITTEE MEMBER LANDOLPH: If they said they

didn't receive it, they didn't receive it. I would assume they act with integrity, so that's not really my business I don't think.

CHIEF COUNSEL MONAHAN CUMMINGS: Well, I understand that. The problem is that the way the statute is written, we have to ask the State's Qualified Experts before we can take these off the lists, even though the agencies that report the information to us, we assume it's accurate. There's no reason for us not to believe that, but we can't do it without you concurring. So that's the only reason we bring it to you. It's an anomaly of the law.

COMMITTEE MEMBER LANDOLPH: It's absolutely bizarre.

CHIEF COUNSEL MONAHAN CUMMINGS: Yes. And every time we do this, it becomes even more anomalous, but it's just the way it is. In order to take this out of the statute, we'd have to have a two-thirds majority of the legislature take it out and find that there's a compelling reason under Prop 65 and just -- we just have to do it this way, sorry.

CHAIRPERSON MACK: -- admit I'm a little uncomfortable because there's not enough information here. We are unqualified experts without knowing a little bit more, and it isn't your fault --

CHIEF COUNSEL MONAHAN CUMMINGS: I'm sorry, but I can't even hear you.

CHAIRPERSON MACK: I said we are unqualified experts because the information given us about this specific chemicals is not enough. We have to take it on faith.

CHIEF COUNSEL MONAHAN CUMMINGS: Exactly.

CHAIRPERSON MACK: If it were written with a page describing this in a little more detail next time, that would help.

CHIEF COUNSEL MONAHAN CUMMINGS: Okay. But what we provided you in the materials before the meeting is a letter from me explaining the process that each of the letters from the U.S. EPA and DPR that gives us this information, and I know that it's a -- it's an odd thing, but the -- but that's all the information we have. And so what we try to do here is just a summary slide that says, based on the information we've already provided you, which is -- was in your packet, DPR says they received these two studies, and we want to take this chemical off the list for those two studies.

CHAIRPERSON MACK: Then I would have appreciated if you'd specify which page, which letter we should have been looking at, because when we look at this, it's -- and so I don't know what I should have been qualified to

read. Next time, please try and do it -- I mean, I'd be happy to vote on it now, because I trust the Department of Pesticide Regulation, whether I should or not.

CHIEF COUNSEL MONAHAN CUMMINGS: All right. So if you want to look at the materials that you have in your -- in your folder, the information is in there. We'll see if we can't get it in more detail next time. What we tried to do is make this a very short part of the agenda because there isn't a lot to it, but --

CHAIRPERSON MACK: If you'd just itemize the letter that we are supposed to have read, because realize --

CHIEF COUNSEL MONAHAN CUMMINGS: Certainly. And it was sent separately to you so that you wouldn't get it too much mixed up with the other materials. It's the only one you received directly from me.

Yes, Dr. Landolph -- I mean Eastmond.

COMMITTEE MEMBER EASTMOND: This is kind of a follow-up. For me, I would feel more confident if you had said the Department of Pesticide Regulation received this study title on this date, and then we would know this is study that was received on that date, and so then you can say, okay, they received it. As it is, it's, you know, it really is going forward on faith.

CHIEF COUNSEL MONAHAN CUMMINGS: Okay. So your

preference would be to know the name of the study that they received?

COMMITTEE MEMBER EASTMOND: Yeah, just -- and when they received it.

CHIEF COUNSEL MONAHAN CUMMINGS: The date and the name of the study? Okay we can do that.

COMMITTEE MEMBER EASTMOND: Basically.

CHIEF COUNSEL MONAHAN CUMMINGS: Sure. I'm not sure that's part of our request, but we will make it that in the future.

CHAIRPERSON MACK: Okay. Now, let's go on faith, and I'll read it again. We'll take the vote.

CHIEF COUNSEL MONAHAN CUMMINGS: Thank you.

CHAIRPERSON MACK: Based on the information that has been provided from the California Department of Pesticide Regulation, should the chemical sodium fluoride, an as identified on slide one, have endpoints removed from list of chemicals required by state or federal law to be tested, but which have not been adequately tested as required? People who will agree that that should happen, please raise their hand.

(Hands Raised.)

CHAIRPERSON MACK: Unanimous.

Next question. Based upon the information which you have been provided from the California Department of

Pesticide Regulation, should the three chemicals identified on slide two have endpoints added to the list of chemicals required by state or federal law to be tested, but which have not be adequately tested as required? The people who assent to that proposition, please raise their hands.

(Hands raised.)

CHAIRPERSON MACK: Unanimous again.

COMMITTEE MEMBER EASTMOND: Could I just clarify. So in this case, we are saying these tests are missing?

CHIEF COUNSEL MONAHAN CUMMINGS: That's correct.

COMMITTEE MEMBER EASTMOND: Okay.

CHAIRPERSON MACK: Third one. Based on the information have been provided from the U.S. EPA, should the three chemicals identified on slide 3 be removed from the list of chemicals required by state or federal law to be tested, in which have not be adequately tested as required? People who assent to that proposition, please raise their hands.

(Hands raised.)

CHAIRPERSON MACK: All right. We are unanimous again.

CHIEF COUNSEL MONAHAN CUMMINGS: Thank you.

CHAIRPERSON MACK: So we are finished with that.

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CHAIRPERSON MACK: Next item. Staff updates. Michelle Ramirez is going to give us staff updates.

MS. RAMIREZ: Hello. Since your last meeting, we've added a total of 11 chemicals administratively for causing cancer and 8 for causing reproductive toxicity. The first slide here shows that for cancer the following chemicals were added: Aloe vera, non-decolorized whole leaf extract; goldenseal root powder; styrene; tetrachlorvinphos; parathion; and malathion. For reproductive toxicity, topiramate was added for the developmental endpoint, and abiraterone acetate was added for all three endpoints -- developmental, female reproductive, and male reproductive toxicity.

This next slide shows that for cancer, the following chemicals were added: Sedaxane; bromodichloroacetic acid -- acid -- pardon me -- 1-bromopropane; furfuryl alcohol; and pentachlorophenol and byproducts of its synthesis in complex mixture.

For reproductive toxicity, atrazine, proprazine simazine, and their metabolites DEA, DIA, and DACT were added for the developmental and female reproductive toxicity endpoints.

On the next slide, we have a list of chemicals under consideration for administrative listing. The far

right column indicates the date of notice of intent to list. There is one chemical under consideration for listing as causing cancer, that is glyphosate. Four chemicals are under consideration for listing as causing reproductive toxicity. That is perfluorooctanoic acid, PFOA; perfluorooctane sulfonate, PFOS; pertuzumab, and vismodegib.

Since your last meeting, one safe harbor level has been adopted in regulation, effective October 1, 2016. The safe harbor is a maximum allowable dose level for bisphenol A, dermal exposure from solid materials.

And on this slide here, as you can see, we also proposed safe harbor levels for eight chemicals. A no significant risk level has been proposed for styrene, and maximum allowable dose levels have been proposed for ethylene glycol (ingested), and for oral exposures to each of the six triazine compounds.

And now I'll turn things back over to Carol. Thank you.

CHAIRPERSON MACK: Thank you, Michelle.

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CHIEF COUNSEL MONAHAN CUMMINGS: Okay. So -- so the update for litigation. Our current case load for Prop 65 is eight cases. We have nine cases total. That have been filing against the office. It's an

unfortunate new record number of cases, but the good news is that we have been successful in defending four of those that are now in the court of appeals, so we were able to get at least trial court wins in four of the cases since, I think, our last meeting. The ones that would be of most interest to you, I think, are in the trial court, we have a case involving the no significant risk level for the chemical chlorothalonil. There's a case filed by Syngenta Crop Protection, and we are still in the negotiation stages on that. We haven't got a trial date yet. May be able to resolve it without a hearing.

In the other trial court case that affects a car -- potential carcinogen is glyphosate is in litigation right now. We were sued by Monsanto Corporation, and that case is pending in the Fresno Superior Court. There's a motion pending on December the 9th. It may resolve the case. It's a constitutional challenge to the labor code listing process, and if we are successful in that motion, the matter will probably go up on appeal.

In the court of appeals, the case -- the only one dealing with a carcinogen at this point is the Committee listing of the chemical DINP, is -- we were successful in defending that at the trial court level,

and that's currently on appeal. It's been fully briefed, and we are just waiting for the Court to set a hearing date on that.

So I don't have other updates at this time, unless you have questions. The rest of the cases all deal with reproductive toxins. Thank you.

---oOo---

ACTING DIRECTOR ZEISE: This is Lauren Zeise. I will summarize the Committee's actions for this meeting. The Committee deliberated on nitrite in combination with amines or amides, and decided that nitrite in combination with amines or amides had not been clearly shown through scientifically valid testing according to generally accepted principles to cause cancer. The decision was unanimous. The Committee also made recommendations to OEHHA to follow up with them on potential subgroups or chemicals within that overall classification, so we heard that the focus should be on those chemicals for which there's human exposures and for which there's positive animal studies. We heard that the nitrosourea -- sorry, not the -- yeah, the nitrosoureas are not -- potentially some of them would be more interesting than others. We also heard about morpholine and aminopyrine, but in general, that we should be looking at those chemicals for which we have

positive results in animals. And Dave Eastmond, do you want to add to that?

COMMITTEE MEMBER EASTMOND: I think, just to clarify, we are talking about the small molecule ureas --

ACTING DIRECTOR ZEISE: The small -- yes.

COMMITTEE MEMBER EASTMOND: Not nitro ureas.

ACTING DIRECTOR ZEISE: Oh, yes, sorry. Okay. Thanks for the clarification. I have nitroso on the brain.

The Committee also reviewed prioritization for five different groups of chemicals. It ranked aspartame as high priority. As medium priority, it rank asphalt and asphalt emissions from roofing, methyl chloride, type-I pyrethroids and vinyl acetate. For the type-I pyrethroids, it expressed a interest in if they come back to them to see them individually as individual compounds.

Did you have something, Gary, that you wanted to say?

MR. ROBERTS: Yes, Dr. Zeise. We disagree with your summary of aspartame. We believe the transcript will not support your summary, and so we want to make sure that our position in understanding is clear for the record.

ACTING DIRECTOR ZEISE: Okay. And my summary was that the Committee ranked it as high priority.

MR. ROBERTS: We disagree. We do not believe the transcript will support that. Our notes do not support that.

ACTING DIRECTOR ZEISE: Okay. So I wonder if we take a pause here and -- Carol?

CHIEF COUNSEL MONAHAN CUMMINGS: I'm going to look at my notes.

ACTING DIRECTOR ZEISE: One possibility is to go back to the Committee. I think we -- that might be faster, to just ask the Committee once again for aspartame. I believe I --

DR. SANDY: I have notes. We can ask the Committee again, but my notes were that Dr. Mack ranked it as high, Dr. Reynolds as high, Dr. Landolph as high, Dr. Dairkee as medium high, Dr. Eastmond as medium high, and Jason as medium; and then they talked about it more after the discussion and came down with a high. That's my notes, but we can --

CHIEF COUNSEL MONAHAN CUMMINGS: I have it as high also.

ACTING DIRECTOR ZEISE: So does anyone on the Committee disagree with this characterization? Martha could you read them again.

DR. SANDY: I think you -- yeah. Took a pole before we started and then after, so I have Dr. Bush, medium. David Eastmond, medium high. Dr. Dairkee medium to high. Joe Landolph, high. Dr. Reynolds, high. Dr. Mack, high. And then a discussion again, and it was high, and a low high.

ACTING DIRECTOR ZEISE: Coming out of the discussion after that initial and what we had was some discussion of the panel, and then we had comment, public comment, and then after the public comment is what we have. So we'll just turn to the panel and ask again.

CHAIRPERSON MACK: The problem is the interpretation of the phrase medium high. If medium high means somewhere between medium and high, that would make problems. What it's intended to mean, I think, is medium in the middle of the high category. At least that's my guess.

MR. ROBERTS: My notes reflect that Dr. Eastmond said medium with flexibility, that Dr. Dairkee said medium -- high within the medium. I confirmed that with her.

COMMITTEE MEMBER DAIRKEE: That is true.

MR. ROBERTS: It is my concern, Dr. Mack, that your impromptu summary at the conclusion of the six votes did not capture what really was a tie, and it is

my further concern that without four votes, it is not accurate under the regulations to identify the outcome as high. Again, I believe the transcript will support this, but since the -- since the -- there is this summary process, I felt it important to share what I heard and what is reflected in my notes.

CHIEF COUNSEL MONAHAN CUMMINGS: Let me just clarify one thing -- well, a couple of things. First off, there is no regulation that has to do with prioritization. There is a prioritization procedure that we use -- an OEHHA procedure, but it's not a regulation. What we are doing when you are doing prioritization is you are giving advice to OEHHA, and it's still our decision what chemicals come before the Committee in what order, so you are giving advice -- whether or not there needs to be a -- a majority vote to give advice, is an open question, so I don't think that four votes are -- votes have required for advice.

In any event, what may be better to do is just to pole the Committee again, Dr. Mack, and clarify what their position was, and we can clarify the record and just move on from there.

CHAIRPERSON MACK: Certainly. But I appreciate you bringing up the issue, Gary. But I also think that that's my recollection also. So let's go through again

and provide our summary.

COMMITTEE MEMBER BUSH: My recommendation was medium priority.

COMMITTEE MEMBER EASTMOND: Mine was medium, with flexibility if it needed to move to high.

CHAIRPERSON MACK: Mine was high with flexibility toward medium.

COMMITTEE MEMBER DAIRKEE: Mine was medium with flexibility toward high.

COMMITTEE MEMBER LANDOLPH: Mine is high.

COMMITTEE MEMBER REYNOLDS: Mine is high.

CHAIRPERSON MACK: There's at least three highs and three mediums; is that right? So we --

CHIEF COUNSEL MONAHAN CUMMINGS: Mic. Mic, please.

COMMITTEE MEMBER EASTMOND: So they just want you to repeat that.

CHAIRPERSON MACK: So I agree it was half and half, three mediums and three highs. So the question is, how to resolve that, and we go to the lawyer and ask her what we should do now.

CHIEF COUNSEL MONAHAN CUMMINGS: I don't think there needs to be a resolution. It's just advice to the --

CHAIRPERSON MACK: Okay. We provided advice to

the staff.

CHIEF COUNSEL MONAHAN CUMMINGS: Thank you.

CHAIRPERSON MACK: And, again, thank you, Gary, for pointing out the problem.

ACTING DIRECTOR ZEISE: Okay. Thank you. So we are one remaining categorization. That's asphalt and asphalt emissions from road paving, which received a low priority.

Okay. So with that, I'd really like to thank the Committee for all the effort and the time it takes to go through the studies, to come to the meeting. Everyone is also so well prepared, and we really appreciate all of your efforts. And I'd like to thank the members of the public and those participating on the web and in the room, and also our staff for all the excellent work that they've done. You can see the documents, and --

PUBLIC MEMBER: I'm so sorry. But, Lauren, you stopped halfway through the prioritization list.

CHIEF COUNSEL MONAHAN CUMMINGS: No, she didn't.

PUBLIC MEMBER: She went all the way through?

CHIEF COUNSEL MONAHAN CUMMINGS: No she summarized all of them. We need to stop interrupting, please.

PUBLIC MEMBER: Yeah, I will do that. I

apologize.

ACTING DIRECTOR ZEISE: Okay. So with that, I'd like to thank everyone in the audience and thank our staff, both scientific staff and legal staff, and the implementation staff for all the hard work.

CHAIRPERSON MACK: There's one person that I didn't thank during this meeting and probably couldn't have been down without, and that's Helen. She did a good job. This was a hard meeting.

ACTING DIRECTOR ZEISE: Okay. Great.

Okay. So with that, I guess we shall be adjourned. Thank you.

(The Carcinogen Identification Committee adjourned at 3:34 p.m.)

C E R T I F I C A T E O F R E P O R T E R

I, JESSICA SOTELO, a certified shorthand reporter of the State of California, 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 by me, and thereafter transcribed under my direction, by computer-aided 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 THEREOF, I have hereunto set my had the 2nd day of December 2016.

Jessica Sotelo

JESSICA SOTELO
Certified Shorthand Reporter
License Number 13679