VIDEOCONFERENCE MEETING

STATE OF CALIFORNIA

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

PROPOSITION 65

DEVELOPMENTAL AND REPRODUCTIVE TOXICANT

IDENTIFICATION COMMITTEE

GOTOWEBINAR PLATFORM

THURSDAY, DECEMBER 10, 2020

10:00 A.M.

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

APPEARANCES

COMMITTEE MEMBERS:

Ulrike Luderer, PhD, MPH, Chairperson

Patrick Allard, PhD

Diana Auyeung-Kim, PhD

Laurence Baskin, PhD

Carrie Breton, PhD

Laurence Baskin, MD

Suzan Carmichael, PhD

Isaac Pessah, PhD

Irva Hertz-Picciotto, PhD

Charles Plopper, PhD

Tracey Woodruff, PhD

STAFF:

Lauren Zeise, PhD, Director

Allan Hirsch, Chief Deputy Director

Carol Monahan Cummings, Chief Counsel

Vincent Cogliano, PhD, Deputy Director, Division of Scientific Programs

Sam Delson, Deputy Director, External and Legislative Affairs

Julian Leichty, Special Assistant for Programs and Legislation, Proposition 65 Implementation Program

APPEARANCES CONTINUED

STAFF:

Francisco Moran, PhD, Acting Chief, Reproductive Toxicology and Epidemiology Section, Reproductive and Cancer Hazard Assessment Branch

Martha Sandy, PhD, Chief, Reproductive and Cancer Hazard Assessment Branch

ALSO PRESENT:

John Acquavella, PhD, Aarhus University

Stewart Averett, AgriTitan, LLC

George Daston, PhD, Personal Care Products Council, Consumer Healthcare Products Association

Donna Farmer, PhD, Bayer Crop Science

Zen Honeycutt, Moms Across America

Tim Johnson, California Rice Commission

Claire Koenig, Adama Agricultural Solutions, Limited

Steve Levine, PhD, Bayer Crop Science

Daniel Minnema, PhD, Syngenta Crop Protection

Keith Morris-Schaffer, PhD, Exponent

Jay Murray, PhD, Murray and Associates

Brandy Riffle, PhD, DABT, Bayer Crop Science

Gary Roberts, Dentons

Jennifer Sass, PhD, Natural Resources Defense Council

Edward Scollon, PhD, Valent USA, LLC

Larry Sheets, PhD, DABT, Bayer Crop Science

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PROCEEDINGS

WELCOME AND OPENING REMARKS

DIRECTOR ZEISE: Good morning, everyone. I'd like to welcome you to this December 10th, 2020 meeting of the Developmental and Reproductive Toxicant Identification Committee. I'm Lauren Zeise. I'm Director of the Office of Environmental Health Hazard Assessment.

And the main agenda item today is prioritization of chemicals for future consideration. That is Committee members are going to recommend chemicals based on a preliminary look at the evidence and exposure potential in California. They're going to recommend them for listing consideration at a future meeting. Proposition 65 listing decisions will be not -- will not be made today.

So this meeting is being recorded and transcribed. The transcript will be posted on OEHHA's website. And we're very glad that we're able to hold this virtual meeting during this time of COVID. We've engaged a GoToWebinar specialist, Jessica Raines, of LogMeIn, Inc. to assist us. And she's now going to give the audience instructions on how to participate in the meeting. So, Jessica.

(Thereupon a slide presentation.)

MEETING MODERATOR: Perfect. Thank you so much for the introduction. So, yeah, I'm going to go ahead and

tell you all about how to participate and go over some housekeeping items. So what we're going to want to do is for the participants viewing the meeting through the webcast, you're going to go ahead and use that link noted there. There will be up to a 10-minute delay. And if you would like to provide public comments, you will need to join the webinar also listed here on the screen.

Now, participants showing the webinar will have an opportunity to provide public comment during today's meeting by clicking on the raise your hand icon. You should be able to see that on the left tab of the GoToWebinar control panel now when the Committee Chair indicates that she is ready for public comment on that item. Now, each commenter will be limited to five minutes or fewer now at the discretion of the Chair. A voluntary online speaker card can be found, also listed here on the screen, which we'll invite you to fill out, if you plan to make a public comment. This will also help us ensure that we've heard from everyone who intends to speak.

Now, if you would like to present slides or have not previously sent them to OEHHA, please email them to the listed email address below now and we will show your slides when it's your turn to speak. Just tell us next slide and advance and we'll go ahead and do that.

Now, if you have a question regarding logistics,

for example, about getting a speaker card or presenting your slides, you may type your questions into the questions pane of the control panel anytime during the meeting. Now, please also by is that this is to assist with issues that may arise in the virtual meeting process, but is not a mechanism for providing public comment.

Now with that, I will go ahead and give the meeting back to the Director.

DIRECTOR ZEISE: Well, thanks so much, Jessica.

NEXT SLIDE

DIRECTOR ZEISE: Now, before we get into the substance of the meeting and I turn the meeting over to the Chair, I'd like to introduce the Committee and staff.

So first, I'll introduce the Committee. And if you could just -- as we're calling your name, if you could just kind of raise your hand so people can see. Your names are probably on everyone's screen, but it's kind of easier to catch if you just hold up your hand.

So first, I'll start. It will be just alphabetically and by last name. So first Dr. Patrick Allard, Patrick Allard, associate professor at the Institute of Society and Genetics, University of California, Los Angeles.

Dr. Diane Auyeung-Kim, Executive Director and head of GRED Non-Clinical Operations and Safety Assessment

at Genentech.

Dr. Laurence Baskin, professor of urology and chief of pediatric urology, University of California, San Francisco.

Dr. Carrie Breton, associate professor of preventative medicine, Keck School of Medicine, University of California -- Southern California.

Dr. Suzan Carmichael, perinatal and nutritional epidemiologist and professor of pediatrics at the Stanford University School of Medicine.

Dr. Irva Hertz-Picciotto, professor of epidemiology and Chief, Division of Environmental and Occupational Health at the University of California, Davis.

And you can't see on your screen yet, Dr. Ulrike Luderer, who is professor of Medicine, School of Medicine, and Director of the Center for Occupational and Environmental Health, University of California, Irvine. And, Dr. Luderer, do you want to say hello. We're having technical difficulties, so if you'd like to say hello.

CHAIRPERSON LUDERER: Yes. Thank you. And hello. And I apologize for the technical difficulties.

DIRECTOR ZEISE: We'll get them sorted out, so.

Okay. And then Dr. Isaac Pessah, Associate Dean and professor of Molecular Biosciences, School of

Veterinary Medicine, University of California, Davis.

Dr. Charles Plopper, Professor Emeritus, Anatomy, Physiology and Cell Biology, School of Veterinarian Medicine, University of California, Davis.

And Dr. Tracey Woodruff, professor, Department of Obstetrics, Gynecology and Reproductive Sciences and Director, Program on Reproductive Health and the Environment, University of California, San Francisco.

So welcome, Committee. Thank you for sharing your expertise today. Looking forward to the discussions.

Now, I'm going to introduce the OEHHA staff. And if you want to turn your camera on as we intro -- as I introduce you and then turn it off after. Allan Hirsch, our Chief Deputy Director; Carol Monahan Cummings, Chief Counsel; Sam Delson, Deputy Director for External and Legislative Affairs; Dr. Vince Cogliano, Deputy Director for Scientific Programs; and from -- good morning -- from the Reproductive and Cancer Hazard Assessment Branch, Dr. Martha Sandy, the Branch Chief; and Dr. Francisco Moran, Acting Chief, Reproductive Toxicology and Epidemiology Section. And then from Proposition 65 Implementation Julian Leichty, Special Assistant for Programs and Legislation.

So I don't see his camera coming on, but welcome staff. And now, I'll ask Carol Monahan Cummings, the

OEHHA Chief Counsel for some introductory remarks.

Carol.

CHIEF COUNSEL MONAHAN CUMMINGS: Thanks, Dr. Zeise. I'm just going to make some general comments now. But I just want to remind you that I can be available for any questions you have. Even if you can't see me, I'm still listening, and so just let me know if you have questions.

As you know, today's meeting concerns the prioritization of chemicals for potential future listing discussions. No chemical listings will be considered at the meeting today. Your discussion and recommendations concerning priority will inform OEHHA's decisions concerning potentially bringing a given chemical to the Committee for future consideration. Such advice is not binding, but is very helpful to us in planning future meetings.

Our scientific staff will explain the process in more detail shortly. OEHHA takes no position regarding whether a chemical should be prioritized or what level of priority that may be, though staff are available to answer questions or locate information for you if needed.

The Governor appointed you, because of your scientific expertise to be the State's qualified experts on reproductive toxicity of chemicals and there's no need

for you to feel compelled to go outside that charge. This Committee can consider human, animal, mechanistic or other data in making a recommendation to OEHHA on the priority of a given chemical.

If you need more information, need more time to consider the evidence or discuss it further before making a recommendation, there is no requirement that you make a recommendation on all two -- all 22 chemicals that are before you at this meeting. We can always hold any chemicals you don't get to over to a future meeting and we want to make sure you have enough time for discussion.

Feel free to ask clarifying questions of me or the other OEHHA staff during the meeting. If we don't know the answer to your question, we will do our best to find it and report it to you. Please, also remember that all discussion and deliberations need to be done during the meeting, not on breaks, lunch or with individual members on or offline, including by a phone, email, in the chats, or text messages or any other way of communicating.

Also, keep in mind that depending on the technology, even on your breaks, there may be the videos and the audio may be available to folks listening, and so make sure you mute and turn off your camera on breaks.

Is there any questions for you -- or for me? For you, there's a lot of questions.

(Laughter.)

CHIEF COUNSEL MONAHAN CUMMINGS: Okay. Thank you.

DIRECTOR ZEISE: Thanks, Carol.

Okay. And now, we'll turn the meeting over to Dr. Luderer, the Chair of the Committee.

CHAIRPERSON LUDERER: Thank you, Dr. Zeise and good morning, everyone. Welcome, Committee members and all the members of the public who are also joining the meeting today.

So as you've heard already, the main item before the Developmental and Reproductive Toxicants Identification Committee today is to advise OEHHA on the priority of 22 chemicals or groups of chemicals for possible consideration for listing at a future meeting. And so the Committee again will not be making any listing decisions today.

So I'd like to now turn to Dr. Martha Sandy and ask her to make a staff presentation giving us an overview of the process today.

Dr. Sandy.

PRIORITIZATION OF CHEMICALS FOR FUTURE REVIEW BY THE DEVELOPMENTAL AND REPRODUCTIVE TOXICANT IDENTIFICATION COMMITTEE(DARTIC)

STAFF PRESENTATYION

DR. SANDY: Thank you, Dr. Luderer.

(Thereupon a slide presentation.)

DR. SANDY And, good morning to everyone. So as the Chair has just said, the main item today that we will discuss is prioritization of chemicals for possible future DARTIC review and listing considerations under Proposition 65.

As several of our DARTIC members have joined the Committee since the last time we brought chemicals for prioritization, which was in 2015, I'm going to give a brief overview of the prioritization process.

Next slide, please.

NEXT SLIDE

DR. SANDY: So the purpose of the prioritization process is to identify chemicals for evaluation of developmental and reproductive hazard by the DARTIC. Specifically, we track chemicals that have some evidence of developmental or reproductive toxicity, which I will shorten to DART for the remainder of this talk and we then prioritizes among this large group of chemicals. The goal is to identify chemicals that you, the DARTIC, should evaluate. We want to focus your efforts on chemicals that are relevant to Californians, so we look at chemicals with apparent exposure in California and then we look at chemicals with the most information that suggests they

might have DART effects.

I want to emphasize that prioritization is a preliminary appraisal of the evidence of hazard. It's not a thorough comprehensive review like what we do when we develop hazard identification materials. The prioritization process is meant to be a quick screen of readily available data relevant to DART for a large number, hundreds of chemicals.

Next slide, please.

NEXT SLIDE

DR. SANDY: So this is a schematic representation of the prioritization process we follow. It's based on the top portion of figure 1 in OEHHA's 2004 prioritization process document that we've provided to you.

Let me walk you through this slide. We maintain a chemical tracking database shown at the top of this slide. And among the chemicals that are tracked, we identify those that have apparent exposure in California and some evidence suggestive of DART. This subset of tracked chemicals is called the candidate chemicals.

We apply focused data screens to those candidate chemicals. By that, I mean we conduct focused literature reviews in order to identify chemicals for which we find positive evidence of DART, either in human epidemiologic studies that meet the requirements of our human data

screen or in animal studies that meet the requirements of our animal data screen.

Chemicals that pass either one or both of these data screens continue further in the prioritization process. There are subjected to a preliminary toxicological evaluation of the overall evidence of DART, taking into account additional information, such as studies on mechanisms of action, metabolism, and pharmacokinetics.

Chemicals for which this preliminary evaluation indicates DART may be a concern are proposed to you for consideration and we consult with you in a meeting like we are doing today. After the meeting, we will consider your advice and OEHHA will select chemicals for preparation of hazard identification materials.

Next slide, please.

NEXT SLIDE

DR. SANDY: So here is a quick recap of our past and present prioritization efforts. We first applied a human data screen to candidate chemicals in the DART tracking database in 2007. For chemicals that passed the human data screen, we looked at the overall evidence by conducting the preliminary toxicological evaluation and we identified eight chemicals with the most compelling evidence to bring to the DARTIC for consultation.

During the next round of prioritization in 2011, we applied an animal data screen to candidate chemicals in the DART tracking database that have been detected in human biomonitoring studies of the U.S. population conducted as part of NHANES, the National Health and Nutrition Examination Study, by the CDC's National Biomonitoring Program.

We brought five chemicals to the DARTIC for consultation at that time in 2011. In 2015, we reapplied a human data screen to 19 chemicals that in 2007 had had some, but not enough, human data to pass the screen. As a result of those efforts, we brought five chemicals to the DARTIC for consultation, in 2015.

In our most recent prioritization efforts, in 2020, we applied both a human data screen and an animal data screen to candidate chemicals in the DART tracking database. For chemicals that passed either one or both of the human and animal data screens, we looked at the overall evidence by conducting a preliminary toxicological evaluation and identified 22 chemicals with the most compelling evidence to bring to you today for consultation.

Next slide, please.

NEXT SLIDE

DR. SANDY: So now, I would like to focus

specifically on the part of the prioritization process shown here in this slide, where candidate chemicals are screened based on evidence of DART. This year in our screening process, we applied both a human and an animal data screen to the results of appropriately focused literature reviews designed to identify studies reporting DART effects in either humans or animals.

For chemicals that pass either or both of those screens, we proceed to the next step, as shown on this slide, in which we conduct a preliminary toxicological evaluation of the chemical. That entails consideration of the overall evidence from readily available information relevant to DART.

Based on these preliminary evaluations, we identify chemicals with the most compelling data as chemicals to bring to you for consideration, consultation, and ranking.

Next slide, please.

NEXT SLIDE

DR. SANDY: This slide summarizes the human data screen that we apply. It is meant to be a quick tool to identify candidate chemicals with some positive findings of DART that have been reported in humans. In order for a chemical to pass a screen, two or more acceptable, analytical, epidemiologic studies reporting adverse

effects for the same major DART endpoint were required.

Next slide.

NEXT SLIDE

DR. SANDY: This slide summarizes the animal data screen that we applied. As with the human data screen, this screen was designed as a quick tool to identify candidate chemicals with a certain minimum amount of relevant DART findings in animal studies. As shown here, there are several ways in which a chemical can pass the animal data screen.

The first is if a chemical has a minimum of one in vivo DART study that meets guideline standards for methodology and reporting and which reports at least one statistically significant DART finding.

The second is if a chemical has a minimum of one in vivo, non-DART, guideline quality toxicity study, such as a cancer bioassay or a chronic or subchronic toxicity study providing statistically significant evidence of at least one DART outcome in accordance with U.S. EPA guidelines for reproductive toxicity risk assessment.

The third is if a chemical has a minimum of five in vivo studies that do not meet guideline standards, but together appear to support a relationship between exposure and one or more specific DART outcomes.

And the fourth is if a chemical has results from

a minimum of one in vitro or non-standard species experiment reporting disruption of essential developmental or reproductive processes combined with in vivo data indicating that the upstream effect would result in one or more DART outcomes.

Next slide, please.

NEXT SLIDE

DR. SANDY: So this slide highlights where we are today in the prioritization process. We are at the stage of consulting with you, the DARTIC, on the 22 chemicals that we have proposed for Committee consideration.

Next slide, please.

NEXT SLIDE

DR. SANDY: And here we have listed each of the 22 chemicals that we are bringing to you today for consultation. And I know this slide is rather -- the writing is small. I'll remind you that this table can also be found on page seven of the prioritization document OEHHA released in October 2020.

Here also, we are characterizing each of the chemicals in terms of exposure. We've characterized them as chemicals having widespread exposure, or having high exposure in frequent consumers, or as having occupational exposures, or other limited exposure. For example, exposure may be associated primarily with recreational or

subsistence fishing, and as having high exposure and infrequent consumers.

Next slide, please.

NEXT SLIDE

DR. SANDY: So today, we are asking you to recommend rankings for these 22 chemicals in terms of priority for preparation of hazard identification materials for possible future DARTIC review and possible listing under Proposition 65.

You will notice that we are asking you to rank these chemicals as either high priority, or medium priority, or no priority. And that's based on the information available at this time. Of course, as new information related to DART toxicity becomes available in the future, these priority Designations can be updated accordingly.

And now, I will turn this over to Deputy Director Dr. Vincent Cogliano to say a bit more about these three priorities categories.

And, Vince, I think you're muted.

DR. COGLIANO: Sorry. Sorry for being muted.

So thank you very much, Martha. So, you have 22 chemicals today, so I'll be brief. Those of you who have been here before me, this is my first meeting, will remember that you've been asked to rank something as

either a priority or not a priority. But with 22 chemicals what we'd like to do is get some sense of which of the ones that are most urgent for us to bring back with the health identification document in next year or in the near future.

So we'd like you to, as you're considering the priority rankings, if you decide that a chemical is a priority for us to develop a health assessment document -- identification document and bring it back to you, the ones that are high priority should be the ones where there's really a good compelling case for DART effects or there's a very good public health case that there's widespread or important exposures that ought to be considered.

Medium priorities are chemicals that are still priorities but maybe don't meet the same criteria for being a compelling case for DART effects or also a high priority for public health impact. And, of course, you can still rank something as no priority if you don't think that it's something that we should be devoting our resources to bringing back before the Committee.

This will help us in determining what chemicals to bring back to you next time. Obviously, if everything is a high priority, it doesn't give us that kind of fine distinction between which ones should we focus on, first, given current data and which ones would be candidates

later.

As Martha just said, this is just based on current data today. Obviously, new studies that come out could change the attention that our staff gives in developing a hazard identification document. So with that, I'll relinquish the floor and wish you a good meeting -- a good and productive meeting and hope that you get through 22 chemicals today.

Thank you.

CHAIRPERSON LUDERER: All right. Thank you, Dr. Cogliano and Dr. Sandy.

So our next step is to begin considering each chemical. So we have kind of rough starting times for each chemical to meet the goal of discussing all 22 of the chemicals in one meeting. However, we can carryover chemicals if that isn't possible, so we can keep that in mind.

So I want to just briefly give an overview of the process by which we'll be discussing the chemicals one at a time. So I'm going to ask each of the lead discussants for each chemical to briefly summarize in one to three minutes their thoughts on the information on the chemical and whether it warrants priority for Committee consideration for listing at a future meeting.

And then I'll open up discussion to others on the

Committee. And subsequently, we'll take public comments on the chemicals, which will be limited to five minutes or less per speaker. And the DARTIC will then further discuss and provide a final recommendation on whether the chemical is viewed as high, medium, or not a priority for consideration by this Committee as a Proposition 65 DART Identification Committee at a fewer -- a future meeting.

And at the end of that discussion, I'll ask for a show of hands for high, medium, and not a priority, and then we'll record those -- those results.

So now I'd like to ask Jessica to go over the public comment process for us.

MEETING MODERATOR: Absolutely. So regarding that, let me go ahead and bring up an information for you. So with that -- let's see here. Give me one second. Now, what you're going to want to do is you just want to make sure if you're going to -- if you want to have any -- say any public comments or anything like that to raise your hand. Remember again, the icon will be next to -- if you're an attendee, it will be next to your name. You can raise your hand and I'll be able to unmute you, so you are able to --

DIRECTOR ZEISE: Excuse me for breaking in, Jessica. Were you putting up a slide or not?

MEETING MODERATOR: Yes, because I have the other

one up, let me bring up that slide again real quick for you. One second. Absolutely.

DIRECTOR ZEISE: Sure.

MEETING MODERATOR: All right. Sorry about that. So that should be the correct slide now that you are seeing. So, yeah, everyone that -- like I mentioned before, make sure to raise your hand on the left-hand tab of the control panel if you want to go ahead and make a public comment. And then also remember, you have the speaker card I spoke to you. You have the link there as well. And we had brought up the slides, if you want to be able to share those, you'd send them to that email that is listed.

And, yes, so go ahead and take a look at this for a few seconds and that's how you'll be able to -- you'll be able to make the public comments there.

Now, would like me to go ahead and put that list up again?

DR. SANDY: I don't think it's necessary at this time.

MEETING MODERATOR: Okay. Thank you.

BENZOPHENONE-3

COMMITTEE DISCUSSION

CHAIRPERSON LUDERER: All right. Thank you, Jessica. All right. Well, we're going to now start with

the first of our -- the 22 chemicals that we'll be discussing today with the benzophenone-3. And the lead discussants for this chemical are Dr. Patrick Allard and Suzan Carmichael. So why don't we start with Dr. Allard.

COMMITTEE MEMBER ALLARD: All right. Yes, good morning, everyone. Can you hear me well?

CHAIRPERSON LUDERER: Yes.

COMMITTEE MEMBER ALLARD: Yes. Okay. Good. Well, first of all, I -- very briefly, I want to say congratulations to the staff of OEHHA for putting such a useful document together. If I can just make one comment, in terms of summary, the often -- for example significance, statistical significance is often mentioned, but not the magnitude of the effects. And as a summary, it would have been great to actually have, you know, the odds ratio or just, you know, the -- again, the magnitude of effect -- the effect size listed, as in the summary of the document.

So for benzophenone, I applied what Dr. Cogliano mentioned, you know, balancing the public health aspect with the amount of data presented. And overall, I rank benzophenone-3 high for several reasons.

So it's an aromatic ketone that's commonly used in sunscreen as well as many consumer products for the purpose of UV protections and protection. And the reason

why I ranked it high was because of its widespread nature. As listed, it's found in the urine of close to 97 percent of people screened in the NHANES survey.

While it's not my specific area of expertise, I did find it concerning that epidemiological data from cohorts in different countries, so completely independent cohorts, reported a positive association between benzophenone-3 exposure and birth weight, which to me suggested an endocrine disruption mechanism, which is supported from the mechanistic aspect of the data.

What I really extracted from the document and from literature mining was -- as a point of significance is really the effect on the thyroid system, specifically decreasing T-3 and T-4. I did find it concerning that this was coming up from human studies, so, for example, the Aker et al. from 2018, as well as in vivo studies, for example, the zebrafish study from Tao et al. from 2020, which I do want to mention was performed at really low exposure levels in the nanomolar range.

So the fact that these studies aligned and there's -- most of these in vitro and other zebrafish studies that also point to an impact on the thyroid system thyroid signaling system for me gave weight and concern in that regard.

And also, there's other endpoints that were

mentioned and of concerns, including an effect in the nanomolar range on oocytes in whole ovary culture, in mice, I believe, which were also of concern. But it was really the thyroid bit that put me overall -- made me overall put the benzophenone-3 in the high category.

And that's the end of my comments.

CHAIRPERSON LUDERER: All right. Thank you, Dr. Allard.

Dr. Carmichael.

COMMITTEE MEMBER CARMICHAEL: All right. Hello, everyone. I agree with Dr. Allard, given that this is a very common exposure in things like sunscreen agents, studies at -- one exposure study estimated 95 percent of residents of LA that they sampled had detectable levels. Similar levels have been found in NHANES.

And then as far as the epi side, there were about 15 studies looking at varied outcomes. So I believe -- and many of them showed suggestive effects. So from that standpoint, I think that we need a further -- a more detailed dive into synthesizing that literature. They ranged in outcomes from mostly birth weight and gestational duration, some on thyroid hormones, age at menarche, placental weight, one-on-one birth defect, sex ratio, childhood fat mass and behavior. So there were -- there were quite a range of outcomes that have been

studied.

So that's my summary.

CHAIRPERSON LUDERER: Thank you, Dr. Carmichael.

I'll now open up this chemical to Committee discussion. Do we have any comments from other Committee members. Please raise your hand and I can call on you.

Okay. I'm not seeing any raised hands.

PUBLIC COMMENTS

CHAIRPERSON LUDERER: We do have one public comment at least. I know one person Mr. Joe DiNardo who has asked to speak during the public comment period.

Do we have any other public commenters who wanted to comment on this chemical?

DIRECTOR ZEISE: Jessica or Julian, do you see any other hands or did you see

MEETING MODERATOR: No, no hands at this time.

CHAIRPERSON LUDERER: All right. Then can -- is Mr. DiNardo going -- have slides or commenting verbally only.

MR. LEICHTY: No slides.

CHAIRPERSON LUDERER: All right.

Mr. DiNardo, are you ready? Or Dr. DiNardo, I should say.

MEETING MODERATOR: Yeah, I went ahead and unmuted him.

DR. DiNARDO: Oh, no. No. Okay. Thank you very much. I appreciate it.

I'd like to thank everybody for at least looking at this compound. It's a very interesting molecule. My colleagues and I have been following it for about six years, specifically more on (inaudible) oral toxicity or embryo toxicity and not coral planula.

So again, I'm just very excited that you're putting this on a high level. The other thing I'd like to just mention to the Committee is that benzophenone-3, or oxybenzone, is used basically in sunscreens. That's (inaudible) percent, which is a fairly high level. Matta and FDA came out with a study in January I think of this year, 2020, and then previous year in February of 2019, which demonstrated its absorption potential.

And again, the molecular weight of the molecule is below or roughly around 228 (inaudible), which is (inaudible).

Other comments that I had is that I'd also like to have the ability to submit documents. There are several other publications that we're missing from the literature mining that you have done. But if that is feasible and you do go ahead and start looking at this molecule a little bit deeper, if there is a mechanism for me to supply information, that would be greatly

appreciated. And that's it.

CHAIRPERSON LUDERER: All right. Thank you very much. We appreciate your comments.

COMMITTEE DISCUSSION AND RECOMMENDATION

Now, we have time for any additional committee discussion?

Would any other Committee -- yes, Dr. Hertz-Picciotto.

You're muted still.

COMMITTEE MEMBER HERTZ-PICCIOTTO: Okay.

CHAIRPERSON LUDERER: Great.

COMMITTEE MEMBER HERTZ-PICCIOTTO: Sorry. I'd forgotten where it was on the GoTo.

Yeah, I just wanted to comment that the fact that the exposure is really quite widespread, and I -- and Patrick gave a good summary kind of overview, but I was just -- in reading over the document from OEHHA, the fact that it's in all these cosmetic products, sunscreen. It's a major -- you know, it's in virtually all sunscreens and not -- very many of them that I've -- when I've looked at ingredients in sunscreen.

And -- and that there are studies showing how it does pass -- that it's found in, you know, in placental tissue, and you know, has -- it definitely is reaching the fetus, and that there's some effects there as well. And

that combined with the thyroid, which of, course, is critical for early development, that thyroid hormone homeostasis is absolutely critical to neurodevelopment, particularly in the -- in the first and early second trimester before the fetus itself is -- is producing its own thyroid hormones to me makes it seem quite important that we take this up.

CHAIRPERSON LUDERER: Thank you, Dr. Hertz-Picciotto.

Do we have any other comments or discussion from Panel members?

All right. If I'm not seeing any hands, then this would be the time for the panel to make final recommendations. So, as I said, I'll ask for a show of hands first for those panel members who believe that this chemical should be ranked as a high priority So please raise your hands and I will say your names.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Hertz-Picciotto, Dr. Carmichael, Dr. Baskin, Dr. Plopper, Dr. Auyeung-Kim, Dr. Pessah, Dr. Woodruff, Dr. Allard, Dr. Breton, and Dr. Luderer. All right. That is a unanimous vote, so we don't need to go on to voting for medium or no priority for benzophenone-3.

BISPHENOL S

COMMITTEE DISCUSSION

CHAIRPERSON LUDERER: So moving on to our second chemical, bisphenol S. For this chemical, the lead discussants are again Dr. Allard and Dr. Woodruff as the other discussant on this chemical. Dr. Woodruff, would you like to start on this one?

COMMITTEE MEMBER WOODRUFF: Sure. I thought I was supposed to look at the toxicology, but can I talk about the epidemiology. First of all, this chemical, BPS, is a structural analog of BPA. And I just wanted to note that this Committee has already voted to declare that BPA is a reproductive toxicant for effects on the ovary at a previous meeting.

BPS is a substitute for BPA. And it's widely detected -- similar to what Dr. Allard said about benzophenone-3, it's widely detected in the U.S. population and appears to be increasing. There is a lot of studies that were identified by the DART. And I guess Patrick will talk about some of the toxicological evidence.

But I just would note, given just -- I would say because it's structurally similar to BPA, we have a lot of studies and there's widespread exposure that I would vote to make this a high priority chemical.

There's studies across multiple endpoints that

are relevant to the Committee. So there's studies that have looked at effects on birth weight as well as gestational duration. And while -- I also wanted to just note that -- that the Committee is doing prioritization and we haven't made a final ruling on all the studies and their evidentiary quality or what they say together. So I -- I appreciate that we have instructions about how to prioritize in terms of is there a lot of studies and do they indicate a direction of effect that is useful for us to consider in terms of a DART committee and a full assessment by OEHHA, but also because of the widespread exposure is another factor that is important for us to consider.

There is also a number -- so there's multiple studies looking at prenatal exposures to BPS with findings on adverse birth outcomes. There's also quite a few studies looking at things like neurodevelopmental outcomes, as well as effects on thyroid. So it will be interesting to see, should this be a high priority chemical, whether this is consistent cross the studies. And I'm going to -- I think, Patrick, you're going to talk. I just -- well, actually, I looked across at the animal studies too, I thought what was interesting about this chemical is that there was a number of studies that looked at developmental exposures and effects on mammary

glands development.

Not sure that's an effect that's been considered by this Committee, but I think it's really something important to consider in terms of developmental exposure and a future effect on health of the offspring. So that to me made this also a chemical that I thought -- in addition to potential reproductive effects such as has been seen with BPS on ovary was something worth -- should be looked at.

CHAIRPERSON LUDERER: Thank you, Woodruff.

Dr. Allard.

COMMITTEE MEMBER ALLARD: Yeah. I mean, I concur. I also ranked it high for several reasons. I think some of the pushback, I guess, against concerns with regards to BPS is the fact that it's still found at relatively low levels in the U.S. But if you look at Asian countries -- some Asian countries like Japan, where it's found at much higher levels, they've actually studied the substitution of BPA a lot earlier than in the U.S. And so the idea is that, oh, one thought is that perhaps in the U.S. we'll eventually catch up and the levels of substitutes to be BPA may actually increase overall in the population.

And I think more concerning is also unfortunately, you know, potential additive or synergistic

effects between still ongoing BPA exposure plus the substitutes. So I think it's worth looking at those BPA substitutes perhaps in a more concerted fashion.

The other thing that I think is really interesting about BPS is some of our own studies, and I hope that's okay to mention, as well as other people's studies, it has structural similarity. And what that actually shows up biologically as is conservation of pathways that are elicited by exposure to BPS, but it's also different.

And so, for example, there's a beautiful study from York et al. in -- from the group of Carol York -- sorry -- in 2016 that exposed human pre-adipocytes to BPS and BPA and compared the two and showed, you know, overlap in pathways, but also distinct responses. And so you can't really look at it specifically and only through the lens of, you know, is it identical to BPA, because it does have distinct effects. So we need to also look at it separately from BPA as well.

So these are the parts that for me, in terms of widespread exposure, the fact that we're likely to be exposed more to it in the future as we have more and more substitution and we have more and more BPA-free products being sold to consumers.

And, of course, the vast array of endpoints that

were listed, and of high concern to me, and again aligning with some of our own results that were not mentioned here in alternative model systems, the fact that sperm and oocyte qualities were strongly impacted in studies that were done at or even below human physiological levels. So all of this together made me rank BPS quite high.

CHAIRPERSON LUDERER: Thank you, Dr. Allard.

We now have some time for Committee discussion. Would any of the other Committee members like to comment on this chemical? Please raise your hands.

Dr. Baskin.

COMMITTEE MEMBER BASKIN: Yes. I agree with Patrick and Tracey. One of the issues kind of more going forward, you know, there's, you know, BPA widespread probably. And all of us have a fair amount of it in our bodies unfortunately. BPS is going to catch up soon. And then the next step is going to be BPM, and, you know, BPE. And the chemical societies, you know, fortunately can, you know, change this quite quickly.

So is there a way to look more globally at this when you make, you know, one amino -- you know, one, you know, change of one carbon molecule in one part of the molecule in one part of structure even though it's relatively similar. You know, it's potentially going to have quite similar, you know, side effects. So as soon as

BPS ultimately gets on the list and we find that it's dangerous, there's going to be BPM. And I guess we're just going to have to stay ahead of the game here.

COMMITTEE MEMBER WOODRUFF: Can I -- can I ask a question.

CHAIRPERSON LUDERER: Thank you.

Dr. Woodruff.

COMMITTEE MEMBER WOODRUFF: Yeah. I did notice that one of the things in -- or one of the items in the materials was - and we do have this for the neonics - is to consider the chemicals as a group. And I don't know -- I mean, no one has really talked about doing that with the BP chemicals as a group. But it might be -- I just was wondering what you thought about that, OEHHA, about thinking about those chemicals as a group. Maybe you -- I mean, it's not -- probably not something to do right this minute, but in like a future thing to think about rather than -- and I think it's a good point that you're just kind of like one-offing these, is that the right way to address it? Kind of like you do with phthalates, for example.

CHAIRPERSON LUDERER: Dr. Pessah.

COMMITTEE MEMBER PESSAH: I just want to make sure. I think that is a good idea for those types of chemicals. But for other chemicals, which are very

diverse, like organophosphates, I think you can't group them, because their affects are, in fact, different and they have different cadres of developmental and neurotoxic effects. So we might want to not generalize totally across all classes of chemicals.

CHAIRPERSON LUDERER: Thank you. Did any -- did any of the OEHHA staff want to comment on that?

DR. SANDY: Yes. This is Martha Sandy. So we would take, you know, your advice into consideration, if you are suggesting we should look at a particular group. I wanted to say that in this particular set of 22, we -- we only have one group we're bringing to you, which is a chemical and its salts, glyphosate and its salts. We did group together three other types of chemicals, but we're asking you to rank them individually.

Now, again, you can give us advice on whether you'd like to see them all as a group or -- and how big a group you'd like us to look at. But at the end of the day, we would, you know, be presenting you with materials, hazard identification materials, in a meeting for consideration for listing and you'd have to make a determination how far you could go in a listing.

CHAIRPERSON LUDERER: Dr. Woodruff, do you have another comment?

COMMITTEE MEMBER WOODRUFF: Well I -- yeah, I

just wanted to follow up on that. I mean, I agree with what you're saying. It just might be -- I mean, I guess we haven't really -- we haven't had -- we've had chemicals come before us where it's like there's a mixture of that chemical and its metabolites that people are exposed to, but we haven't really had a structure to think about chemicals as a group. And I feel like it's worth thinking about, because we're exposed to them as a group and together they could affect the same endpoints with the caveat that sometimes they have different endpoints. And I know we have many chemicals to go through today, but I do think it's something worth, like exploring as a more efficient way to approach this for future evaluation and discussion, but that's my recommendation on that, I guess.

CHAIRPERSON LUDERER: Thank you, Dr. Woodruff.

Dr. Breton.

COMMITTEE MEMBER BRETON: Hi. I just wanted to follow up with Tracey's comment, because I think as we, you know, progress in the scientific literature too, many of these chemical families are being evaluated together in mixtures modeling approaches too. And so it's going to be that much harder. Like, they're being evaluated together, and they're -- so it's going to be harder to just -- to critique them separately, as more and more literature is actually looking at them together.

CHAIRPERSON LUDERER: Thank you.

PUBLIC COMMENTS

CHAIRPERSON LUDERER: Let's see, I don't see any other hands in the Committee. Do we have any public comments, anybody who requested to comment on this particular chemical?

MEETING MODERATOR: I'm not seeing any comments or hands raised on my end here.

CHAIRPERSON LUDERER: All right. Thank you, Jessica.

COMMITTEE DISCUSSION AND RECOMMENDATION

CHAIRPERSON LUDERER: Do we have any further Committee discussion on Bisphenol S?

All right. Then seeing no additional hands, we can move on to our final recommendation. So again, I'll ask everyone to raise their hands. First, we're going to be voting on classifying this in the high priority category. So please raise your hand hands and I'll call your names.

(Hands raised.)

CHAIRPERSON LUDERER: All right. Dr. Hertz-Picciotto, Dr. Baskin, Dr. Carmichael, Dr. Pessah, Dr. Auyeung-Kim, Dr. Woodruff, Dr. Allard, Dr. Breton, and Dr. Plopper, and Dr. Luderer.

All right. So the vote again was for this

chemical bisphenol S was unanimous among the Committee members.

DIAZINON

COMMITTEE DISCUSSION

CHAIRPERSON LUDERER: Let's see, I think, yes, we certainly have time for -- to move on to one additional chemical before we need to take a break. So the next chemical is diazinon. And the lead discussants for this chemical are Carrie Breton and -- Dr. Breton and Dr. Pessah. Dr. Breton, would you like to go first?

COMMITTEE MEMBER BRETON: Sure. Okay. So diazinon -- so this is a widespread organophosphate insecticide. It was banned for residential use since 2005, but still used widely in agriculture. In terms of the human epi data, there are a couple different outcomes that have been evaluated with this chemical. But generally speaking, there's only one to two epi studies for each outcome.

So when I was looking at that, I kind of felt that the evidence for birth weight for instance is fairly equivocal. There's one study that found an association, another one that did not. The evidence for neuro outcomes, specifically autism spectrum disorder and just measures of cognition is probably the most compelling, although it's still limited in the number of studies that

have actually addressed these outcomes.

And then the evidence for reproductive effects is also suggestive and supported in addition by similar effects that are observed in rat studies. So on the whole, given the fact that it's -- it's been banned and that the body of evidence is still somewhat small for individual outcomes, I ranked this as a medium.

CHAIRPERSON LUDERER: All right. Thank you, Dr. Breton.

Dr. Pessah.

COMMITTEE MEMBER PESSAH: Thank you. I focused on the animal studies. It's very well known that diazinon as an organophosphorothioate is essentially designed to be a neurotoxicant through its activity on acetylcholinesterase and cholinergic systems. But the most -- more recent literature indicates that it has other effects that may be different from organophosphate induced acute toxicity. And these are possibly effects on serotonergic systems, which would, in fact, reinforce some of the epidemiology studies that suggest impacts on social -- development of proper social behavior.

It also seems to impact long-term expression of key receptors, not only serotonergic but also cholinergic receptors. The data, which is most compelling in rats that has come out of Duke in the last couple of years,

which infuse different paradigms, pulsatile versus constant infusion into pregnant dams, mainly rat studies, which produced quite significant developmental outcome in the offspring, including changes in risk-taking behavior and impairing novel object recognition, as well as having some cognitive decrements in the offspring.

So I tended to rate it, based on the animal studies, a bit higher than my colleague.

CHAIRPERSON LUDERER: Thank you, Dr, Pessah.

We have time for Committee discussion at this point.

Dr. Woodruff.

COMMITTEE MEMBER WOODRUFF: Yeah. I just wanted to clarity, it didn't -- it's been banned for residential use, but it's still being used agriculturally in California and it's quite widely used, right? So there's -- I think the thing which we had commented on before, which is that there's widespread population exposure to like benzophenone-3 and increasing to BPS, but that this one would be a concern, it seems like, for people who are working with it agriculturally. So occupational exposures and agricultural workers, I assume would have exposures to this chemical and that would -- and probably higher exposures. So I think that would warrant concern about having us evaluate it or having high

priority for it, I guess, even the animal studies that Dr. Pessah talked about and are in the documents.

CHAIRPERSON LUDERER: Dr. Pessah.

COMMITTEE MEMBER PESSAH: Yeah, there is a study from the CHAMACOS which, you know, is a Berkeley-based study, but it's actually, at least in one county that they studied, Monterey County, it has the highest application rate of any of the organophosphates, kilograms used within one kilometer of residents during pregnancy. So the risk for developmental toxicity is there, because the exposures are there, both through oral intake as well as dermal and pulmonary intake, it is volatile.

CHAIRPERSON LUDERER: Any other comments from the Committee? Yeah, I wanted to also underscore that, that in these -- in the agricultural communities, the exposure is not only occupational, but I think also residential, due to living in closed proximity to areas where it's applicate -- applied.

All right. Thank you.

Do we have any public comment requests for diazinon.

Oh, Dr. Hertz-Picciotto. I'm sorry. I didn't see your hand there for a minute.

COMMITTEE MEMBER HERTZ-PICCIOTTO: Yeah. I -- I find it -- this is -- this chemical, of course, has been

around for a very long time and has had -- you know, I mean and it's used globally in a big way. I think it's been maybe substituted with others -- other -- other organophosphates in its uses for the -- what used to be the home uses of course. And yeah, I find that, even though it's not a lot of studies in humans, which is a little surprising given how long it's been around, but what's there actually looks pretty compelling as a basis to let's move forward.

I'm also impressed that, you know, one of the big questions has been what is the mechanism for these longer term chron -- you know, these developmental effects from prenatal exposure. So much attention has paid to, you know, the acute toxicity and, you know, cholinesterase inhibition. And even that ends up being pulled up politically as well. There's not any poisonings going on anymore, because we, you know, cleaned up that part of the agricultural experience, which is not really true, but it's still going on.

But I think it's been a bit of a quandary, you know, really trying to pin down even for chlorpyrifos what is the mechanism by which, you know, it induces these neurodevelopmental effects from prenatal exposures. And so I thought it was really interesting what you were saying, Dr. Pessah, about the serotonergic and some other

mechanisms that -- that the evidence seems to be converging around.

So I find that to be another argument for kind of raising it in -- not that we need to know the mechanism necessarily, but that that helps -- helps to buttress the argument for putting this as a high priority.

CHAIRPERSON LUDERER: Dr. Allard.

COMMITTEE MEMBER ALLARD: Yeah. I also picked up on the serotonergic aspect of it. And what I think is interesting is, you know, in going in line with what we just said and mentioning chlorpyrifos, chlorpyrifos is another organophosphate that is not just working through cholinergic system and there's evidence in rats that -- or pretty compelling evidence in rats that it also affects the serotonergic systems.

So talking about, you know, the specificity of the chemical for the cholinergic system is -- as the only mode of toxicity would not necessarily be reasonable as an argument to make, because it seems to -- these organophosphates seem to be affecting the serotonergic system as well, and we need to be considering this for evaluation. That's my take.

CHAIRPERSON LUDERER: Thank you.

PUBLIC COMMENTS

CHAIRPERSON LUDERER: Jessica, do we have any

requests for public comments?

MEETING MODERATOR: We actually do. So it's going to be Claire Koenig. And Claire, I'm going to go ahead and unmute you now. You are still self-muted, so once I click it, go ahead and click it on your side as well.

MS. KOENIG: Hi. Can you hear me now?

CHAIRPERSON LUDERER: Yes.

MEETING MODERATOR: Yes.

MS. KOENIG: First, I just want to thank the Committee for taking the time to do their due diligence and review the database for diazinon. I'm speaking today on behalf of Adama Agricultural Solution Limited.

And the point I wanted to raise during my comment specifically is about exposure for Californians. Since the commenting period closed, it came to the attention of Adama that implementation of the federal agency's Endangered Species Act will ultimately lead to the eventual cancellation of the majority of diazinon agricultural uses in California and ultimately thus a reduction in human exposure potential.

While the timeline for implementation has not been solidified, I thought this was relevant for consideration during prioritization of the molecule by the Committee. And that's it.

CHAIRPERSON LUDERER: Okay. Thank you for your comment.

COMMITTEE DISCUSSION AND RECOMMENDATION

CHAIRPERSON LUDERER: Do we have any further discussion by the Committee -- members of the Committee?

All right. Then we can move on to the final recommendation. So again, I will ask for a show of hands for each of the possible vote -- categories in which we can place diazinon. So please pray -- raise your hands if you vote to make this a high priority chemical or recommend that it become a high priority chemical.

(Hands raised.)

CHAIRPERSON LUDERER: All right. Dr. Hertz-Picciotto, Dr. Baskin, Dr. Carmichael, Dr. Pessah, Dr. Auyeung-Kim, Dr. Allard, Dr. Plopper, Dr. Woodruff, and Dr. Luderer. All right.

So do we have any votes for medium priority?

(Hand raised.)

CHAIRPERSON LUDERER: Dr. Breton.

And I think that is everyone on the Committee. So we have one vote in the medium priority and the remaining votes in high.

All right. Thank you.

DIETHYL PHTHALATE

COMMITTEE DISCUSSION

CHAIRPERSON LUDERER: We can then -- we're making very good progress here. We can then move along to diethyl phthalate. So the lead discussants for diethyl phthalate are Dr. Baskin and Dr. Woodruff.

Dr. Baskin, would you like to begin?

COMMITTEE MEMBER BASKIN: Yes. Can everybody hear me?

CHAIRPERSON LUDERER: Yes.

COMMITTEE MEMBER BASKIN: Okay. Let me just grab my -- okay. So this one is also a little bit problematic in the sense that when you want to study one phthalate, you're going to be trying to study all of them, and you're going to be studying, you know, all the metabolites. You know, but saying that, I was able to, you know, look at a number of these papers. And quite frankly, I felt -- I felt that there was actually a relatively low reason to list this. There were a few animal studies, some showed that there, you know, may be an effect. But a lot of confounding variables. And most of the studies actually didn't really relate to reproductive, you know, issues related to the phthalates.

Probably the once -- the one study that was potentially most interesting was from the National Toxicology Program way back in 2006 when they did, you know, a huge analysis of all the papers from that time

earlier. And the human study, which, of course, is of most interest could really be questioned in terms of its methodology. And the animal studies weren't, you know, particularly conclusive.

There was also a WHO study back in 2003, which, of course, showed some subtle changes in sperm analysis, sperm concentration. But, of course, as has been typical really no change in fertility, so it's unclear whether that relates to phthalates or the million of other things that we're exposed to.

So in summary, I had actually a low sense here that this should be looked at for further issues based on the studies given.

CHAIRPERSON LUDERER: Thank you, Dr. Baskin.

Dr. Woodruff.

You're muted it looks like.

CHAIRPERSON LUDERER: No, we still can't hear you.

No. We still cannot hear you. I wonder if we can get some technical help possibly.

COMMITTEE MEMBER ALLARD: You're going through your phone, Tracey, right?

MEETING MODERATOR: Yeah. So I have -- she joined through the phone. So I just sent her the pin number, so we're able to unmute. I just sent it again.

And, Tracey, if you can hear me, the pin number is pound 71526 pound.

Yeah. It looks like she got switched over to phone. I'm going to go ahead and assist her real quick.

CHAIRPERSON LUDERER: All right. In the meantime, do we have any other -- any discussion or comments from the Committee at this point?

Dr. Allard.

COMMITTEE MEMBER ALLARD: Yeah. I mean, it's clear that it doesn't have the same potency as other types of phthalates, like DHP. What I think was striking from the in vivo data I presented is that a lot of it showing positive effects was collected at extremely high levels, so we're talking about in the gram per kilogram per day, 15,000 ppm. So I -- I ended up, you know, sort of leaning also towards, I guess, more of a low than a no. I wish there was a low category as opposed to no to medium.

But, yeah, so in the category that does not exist, I was -- I was ranking towards a low.

COMMITTEE MEMBER PESSAH: I think I put it in the low category even though that doesn't exist, Patrick.

CHAIRPERSON LUDERER: Thank you.

COMMITTEE MEMBER WOODRUFF: Can you hear me now?

CHAIRPERSON LUDERER: Yes, we can hear you now.

COMMITTEE MEMBER WOODRUFF: Okay.

CHAIRPERSON LUDERER: Go ahead.

COMMITTEE MEMBER WOODRUFF: I just wanted to say that while I agree that the studies are not -- let me turn this off. There is some challenges with them, actually there's widespread exposure to the phthalates. So I think that made me concerned that it is -- while I wouldn't say there's no concern about this, I would say it is possibly medium in terms of having a look at what -- the studies that have been done. I think there's going to be more studies of this as this is -- the science evolves, because there's -- this chemical is, you know, widespread and there is some concern about the -- that there is sometimes effects found in the human studies that are not seen in the animal studies, so there might be some differences between the two groups.

So, I mean, I agree that the science is not as compelling as the previous chemicals we discussed, but I still think it's worth keeping it on the radar for OEHHA, given that there's widespread exposure to it.

CHAIRPERSON LUDERER: Thank you, Dr. Allard -- Dr. Woodruff, sorry.

PUBLIC COMMENTS

CHAIRPERSON LUDERER: Do we have any comments -- any public comments, Jessica?

MEETING MODERATOR: I am not seeing any hands

raised at the moment. As for -- let's see here in the questions pane. No, not at this time.

CHAIRPERSON LUDERER: All right. Thank you.

COMMITTEE DISCUSSION AND RECOMMENDATION

CHAIRPERSON LUDERER: Do we have any further discussion from the Committee?

Dr. Hertz-Picciotto.

COMMITTEE MEMBER HERTZ-PICCIOTTO: Yeah, this is something of a question for the OEHHA staff. And so as I'm noticing in your document, you know, there's this Table 3, which is basically about exposure levels, in a variety of different studies. And then many of those studies, they're -- they're not -- there's nothing reported under human epidemiologic studies. So I was just wondering whether -- that there were null studies that you just -- you didn't actually list in where you're going through the evidence, and -- because that -- you know, whether -- whether there's no studies versus there's studies that actually have null findings to me, it's kind of -- it makes a difference in how I -- how I view it.

DR. SANDY: So this is Martha Sandy with OEHHA.

As we said in this particular summary for DEP, we looked at epidemiologic studies that we identified within the last -- with an emphasis on those published in the last two years. This again we're screening many, many

chemicals. It's not a comprehensive literature search. So these are the studies that came to our attention. We -- we are not saying that we've -- it's a comprehensive list.

CHAIRPERSON LUDERER: Thank you, Dr. Sandy.

And I would add that there are other epidemiological studies earlier than the last two years.

Dr. Breton.

COMMITTEE MEMBER BRETON: Yeah. I actually wanted to ask another -- a clarifying question too as we're going through these. And so I approached these a little bit as -- my assumption is that it's not going to be beneficial if all of the chemicals on this list are ranked high, because then we haven't helped you in any way, right?

So I just want clarification that that -- I mean, that's how I approached the whole list of chemicals. So I -- you know, so they were definite -- they were -- you know, the evidence that I had to work with I ranked in my mind relative to the other sets of chemicals to be able to have some low, some medium, and some high. So I just kind of want to get a sense from you that that -- I approached -- you know, that that was a reasonable approach in this.

CHAIRPERSON LUDERER: Dr. Sandy, could you

perhaps comment on that?

DR. SANDY: Yes. I'll let -- as Dr. Cogliano had said earlier, yes, that it is much more helpful if we get your sense of what are the most important chemicals to bring to you in the future for listing consideration. So if they were all given the same priority, that would not be very helpful to us.

COMMITTEE MEMBER BRETON: Okay.

CHAIRPERSON LUDERER: Dr. Woodruff, you had an additional comment.

COMMITTEE MEMBER WOODRUFF: Well, yeah, I just was -- I just wanted to know -- follow up, because Martha said that the epi studies only -- or even the animal studies only cover the last two years, and this chemical has been studied for a while, which I think Dr. Baskin has talked about a little bit. And I -- I had a question just following up on the comment about the priorities. Well, actually how many chemicals do you think you would -- after you get the recommendations, do you think you'll do over the next, is it like year or two from this list. And if something comes up, say somebody publishes a bunch of stuff on say this chemical, would that then come back to the Committee and say, oh, my gosh, look at all this new staff or we could tell you that?

DR. SANDY: Prioritization is an ongoing process.

And we realize there are new studies coming out all the time that can raise the concern or lower the concern about different chemicals. So we do take all of that into account. And we may choose to bring something to you that is clear. We may consult with the Chair as we did with cannabis, for example -- cannabis smoke recently.

COMMITTEE MEMBER WOODRUFF: Oh, right. I remember that.

DR. SANDY: Or we may bring -- you know, prioritize it again and bring it back to you. It will depend on the circumstances, the data that are available.

So back to what -- how many years we're looking. If there's a lot of literature, and we think it -- just looking in the last two years. So for -- we -- we tried to spell it out. We emphasized the epi studies for the last two years. We don't have that same statement for DEP when we talk about the animal studies. Okay. So we didn't limit it to the last two years.

We -- again, we're not claiming that we have done an exhaustive literature search for all studies that are relevant on DART effects for DEP. That would take us too much time and defeat the purpose of tying to do a quick prioritization screen to identify the ones that we think are important to look at.

CHAIRPERSON LUDERER: Thank you. That's very

helpful. Dr. Baskin, you had a comment as well.

COMMITTEE MEMBER BASKIN: Yes. I was just going to make sure I understood this. Are we voting like high, medium, low now, is that kind of what you want from us, because a I agree with the prioritization. We can't just say all 25 of them, you know, are dangerous. I mean, oxygen is dangerous if you get it in too high of a level and we're certainly not going to study that, so just a little bit of guidance.

DR. SANDY: We would like to hear from you if you think there's a chemical that right now you don't think should be given a priority based on the evidence we know now. And then we find that a low priority is not very helpful, because a low is kind of like a no. We'd like to -- thinking that this is an ongoing process, and science evolves, and there's always new information, right?

So really, what do you think are the highest priority chemicals for us to focus on. And then what's something else that's also really important, you think it's compelling to bring it to you some time, but it's a medium. It's slightly lower priority. And then which ones are -- have less priority, so we'd like those to be a no for now.

COMMITTEE MEMBER BASKIN: Got it.

DR. SANDY: And I'll turn to Dr. Cogliano if he wants to elaborate on what I've just said.

COMMITTEE MEMBER BASKIN: So as scientists, you know, we're always going to find, you know, some concern. There's, you know, P values. You know, there's level of evidence. And so you're basically telling me that I should probably say no for this one, because I didn't think it was -- I thought it was low but you don't want to give me a low, so I'm going to say no. But I like the way that you've -- I get it, where the other ones it was clear. Like, yes, I'm worried about it. So I get it, so I think that was very helpful.

COMMITTEE MEMBER AUYEUNG-KIM: But there's (inaudible), where if we do say no to this, that if more data comes out, you can prioritize it, correct?

CHAIRPERSON LUDERER: Yes.

DR. SANDY: Yes

DR. COGLIANO: Yes, absolutely.

CHAIRPERSON LUDERER: Dr. Pessah.

COMMITTEE MEMBER PESSAH: I also -- because I heard that diazinon may be actually registration ceased due to Endangered Species Act, that I wasn't aware of, that that one has made it into the high category. But should that cancellation of registration occur and the ramp down period is relatively quick, diazinon doesn't

persist in the environment and so we may want to take it off the list, depending on what the circumstances are.

CHAIRPERSON LUDERER: And the staff can comment on that. But I assume that that would be something that staff would be taking into account when they're deciding when chemicals to bring to the Committee for listing, correct, Dr. Sandy?

DR. SANDY: That's correct. That's correct.

CHAIRPERSON LUDERER: Thank you.

Dr. Woodruff, did you have another comment?

COMMITTEE MEMBER WOODRUFF: No.

CHAIRPERSON LUDERER: All right. Do we have a -- any public comments?

MEETING MODERATOR: I am seeing no hands or comments at this time.

CHAIRPERSON LUDERER: All right. Thank you. Then we can go on to our -- making our final recommendation on diethyl phthalate. So I'll -- again as before, I ask everyone on the -- anyone on the Committee who would put this in the high priority category to please raise your hands.

(No hands raised.)

CHAIRPERSON LUDERER: Okay. I see no hands for high.

The medium priority?

(No hands raised.)

CHAIRPERSON LUDERER: I am seeing no hands for medium.

No priority?

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Hertz-Picciotto, Dr. Baskin, Dr. Carmichael, Dr. Pessah, Dr. Auyeung-Kim, Dr. Allard, Dr. Breton, Dr. Plopper, Dr. Woodruff, and Dr. Luderer. So that's all the Committee members voted to not prioritize diethyl phthalate.

All right. So I believe now is the time when we need to take a break for 10 minutes. It's 11:20. So unless there's something -- is there anything that the staff would like to bring up before we take a break? We'll take a break for ten minutes until 11:30.

CHIEF COUNSEL MONAHAN CUMMINGS: Yeah. This is Carol. I just want to remind everybody that it's possible that you could be seen or heard, so if you want to turn off your camera and your mic, while you're on break, that's great. And just a reminder not to communicate with each other on these chemicals that you're looking at today.

Thank you.

CHAIRPERSON LUDERER: Thank you very much.

All right. We'll see everyone again at 11:30.

Thank you.

(Off record: 11:20 a.m.)

(Thereupon a recess was taken.)

(On record: 11:33 a.m.)

DOMOIC ACID

COMMITTEE DISCUSSION

CHAIRPERSON LUDERER: All right. So now we can go ahead and get started moving on to the next chemical for discussion, which is domoic acid. And the lead discussants are Dr. Pessah and Dr. Hertz-Picciotto. Dr. Hertz-Picciotto, would you like to start this one?

COMMITTEE MEMBER HERTZ-PICCIOTTO: Okay. I was actually hoping that Dr. Pessah would start.

CHAIRPERSON LUDERER: We can do that.

COMMITTEE MEMBER HERTZ-PICCIOTTO: There is no human epidemiologic evidence, but I'll just give it kind of opening thing, which is that, you know, Domoic Acid is produced by harmful algal blooms, which are becoming more and more common along the Pacific coastal waters. And to my understanding actually OEHHA and others at the State Health Department have kept this problem at bay with regard to our food supplier -- our seafood supply through very, very close monitoring of the waters, and the fisheries, and so forth along our coast.

There are some studies I noted that are on

ongoing. One of them is in the Washington area with the Native American populations that these -- I forgot what kind of plants they are -- the name of it, but it's a really important part of their cultural heritage. And that is one population that has had some very high exposures and there are some studies now ongoing there.

Our environmental health sciences center did sponsor a workshop of scientists on domoic acid. But at this point, I don't see a particular -- you know, any imminent issues in regard to human health, partly because of what's in place currently for monitoring. And, you know, the data on wildlife is actually pretty compelling. That's the -- it's a terrible neurotoxin. And, you know, beaching sea lions and many other sea mammals where -- who have to eat the seafood - that is their source of sustenance - have been suffering quite greatly. But as far as human exposures, I think, at least as far as California goes, I don't see that being any kind of major issue to be taken up. That's it.

CHAIRPERSON LUDERER: Thank you.

Dr. Pessah.

COMMITTEE MEMBER PESSAH: So I would have to agree about the exposure and the sort of the monitoring that, you know, tries to restrict exposure through seafood. That's clearly a regulatory sort piece that

limits exposure. And then unfortunately I read the Burbacher studies that just were published a few weeks ago or maybe a few months ago in the non-human primate, where they adjusted doses to the near regulatory levels. And the neurotoxicity and the developmental toxicity that they report were really troubling actually.

These were in utero exposures in non-human primates and they looked at a number of behavioral outcomes, as well as imaging of the brain and other metrics of hippocampal health and they found some rather, you know, dramatic differences at these exposures, which are near the regulatory levels. And so I don't know if there's single regulatory level across states like I'm sure they were referring to maybe Washington State regulations. But if not, and if we're all kind of in the same ballpark in terms of the monitoring and then the flags going up for seafood content of these, domoic acid, this is one chemical we know a lot about the mechanism of action. And we know that that mechanism causes harm, both developmentally, because domoic acid crosses the placental barrier, but also the very high sensitivity of the developmental stages to domoic acid.

So I would have actually placed it in the medium category, if it wasn't for these recent studies that seem to raise flags about very low levels that are near current

regulatory warning levels. So I moved it up to high. Sorry.

CHAIRPERSON LUDERER: Thank you. And those are studies that are not in the document, is that correct?

COMMITTEE MEMBER PESSAH: I'm sorry?

CHAIRPERSON LUDERER: Those are so new that they're not -- they haven't -- weren't reviewed for this document, to clarify.

COMMITTEE MEMBER PESSAH: No, they're not in -- no, they're not in it.

CHAIRPERSON LUDERER: Yes, right. Just wanted to make sure that everyone understood that.

Dr. Woodruff, do you have -- did you have a comment? I thought I saw you raise your hand.

COMMITTEE MEMBER WOODRUFF: No, I didn't raise my hand.

CHAIRPERSON LUDERER: Okay.

COMMITTEE MEMBER WOODRUFF: But I do have a question though, since you called on me. So in this -- one of the factors for considering this is kind of public health significance. And I -- I guess I'm wondering how -- if we looked at the chemical, how that change -- because the State of California is already doing pretty intensive monitoring and evaluation for this toxicant, because of the seafood implications.

So I don't know. To me, some of the other chemicals we're looking at are not being paid attention to as much in the regulatory process, so it has more of a public health significance that we -- we recommend it for high. So I wasn't completely sure. I know we're just weighing in on the science. But I know OEHHA is involved in this regulatory compliance. Maybe they could comment on what happens if it's listed, how that changes what's going on?

CHAIRPERSON LUDERER: Dr. Sandy perhaps or Dr. Cogliano.

DR. COGLIANO: This is Vince Cogliano. I'll -- Go ahead, Martha, were you going to -- No.

Yes. As you pointed out, OEHHA and the State of California has a strong program of monitoring domoic acid in shellfish. It has made fisheries closures/reopenings based on levels of domoic acid. And it's based on the -- right now on the neurotoxic potential and it's a very strong neurotoxicant as also been mentioned.

If it were listed under Prop 65, that would be part of the scientific justification for a fee for potential fishery closure. And if we developed a maximum acceptable daily level, or a MADL, if that became more important than the neurotox standard, we would -- it could potentially change the -- change the level. But right

now, we do have an active program. We've closed fisheries because of high levels of domoic acid in shellfish and will continue to do so.

COMMITTEE MEMBER HERTZ-PICCIOTTO: Do you know -- Martha, anything to add or Lauren?

COMMITTEE MEMBER HERTZ-PICCIOTTO: Also, if one of you can address the issue of -- and I understood that there has been discussions among the State health departments of, you know, Washington, Oregon, California are -- is our current regulatory standing the same as what Washington, because that's apparently what the Burbacher paper, it sounds like, used as their -- you know, their measure of exposure in the non (inaudible) studies.

DR. COGLIANO: I'm not prepared to discuss the levels of the other specific states. I know that the states do coordinate very closely on how they look at domoic acid. I can find that information out and get back to you.

COMMITTEE MEMBER HERTZ-PICCIOTTO: It seems relevant to this decision.

DR. COGLIANO: Okay. Well, I will --

CHAIRPERSON LUDERER: Thank you.

DR. COGLIANO: I will check then on the levels of the other -- of the other Pacific states and how they compare with California's levels and take a little bit of

time to get back to you.

CHAIRPERSON LUDERER: Okay. Thank you.

Dr. Carmichael.

COMMITTEE MEMBER CARMICHAEL: And I just want to just once again be clear about what our call is. I mean, because there's a lot -- there's multiple levels of deciding what actually comes for full review, right? And this is -- this is just one level. So even if hypothetically we said that all of these were high, then OEHHA then takes all these types of things into consideration, some of which we really aren't called to figure out, I guess, to decide then a priority for full review. Like, it came up with diazinon also, for example.

DR. COGLIANO: Yes. As Martha had said earlier, prioritization is an ongoing process. So, yeah, this is one factor and it's as of today. If other information comes out, if it becomes clear that this is of higher or lower public health importance to bring it to the Committee, that would factor into our decision.

COMMITTEE MEMBER CARMICHAEL: And that's where I thinking about the low versus -- or the -- I started thinking about low versus no. I kind of think of the no as low, because all of these were brought to us in the first place, because there was some -- some evidence of concern. So just trying to put -- put all this into

perspective.

DR. COGLIANO: Right. The reason for have -- not having a low priority category is the -- just to be clear, if you were to tell me that something is low priority, I can't interpret that as saying don't really work on that right now. This isn't -- its --

COMMITTEE MEMBER CARMICHAEL: Okay. That's fair enough.

DR. COGLIANO: So low priority is a bit of a mixed message. So we want to void that to be clear.

COMMITTEE MEMBER CARMICHAEL: Got it.

CHAIRPERSON LUDERER: Okay. Thank you.

DR. COGLIANO: Thank you. I will go check on the domoic acid and get back.

CHAIRPERSON LUDERER: All right. Do we -- I guess one of -- the question is do we want to wait for that information before making our final recommendation on this chemical.

PUBLIC COMMENT

CHAIRPERSON LUDERER: But before we talk about that, I just want to ask Jessica if there are any public comments on domoic acid?

MEETING MODERATOR: At this time, there are no hands raised.

CHAIRPERSON LUDERER: All right. Is there a

recommendation from staff about whether we should move on to the next chemical and delay the vote until we have additional information do the panel members have an opinion about that?

COMMITTEE MEMBER HERTZ-PICCIOTTO: I would prefer to wait before voting.

DR. SANDY: This is Martha Sandy with OEHHA. I think we'll have that answer for you in a little while, after the next chemical.

CHAIRPERSON LUDERER: Okay. Great. Then we will do that. Thank you.

GLYPHOSATE

COMMITTEE DISCUSSION

CHAIRPERSON LUDERER: All right. Well, the next chemical is glyphosate and it salts. And the lead discussants for glyphosate are Dr. Breton awe Dr. Plopper.

Dr. Breton, would you like to begin?

COMMITTEE MEMBER BRETON: Okay. Sorry. Let me get my notes. All right. So glyphosate and its salts. This is a very widely used herbicide across, you know, certainly California and the country.

The literature, in terms of the human literature, this -- the literature provided in the report was from the last five years. And so in looking at that literature, the evidence is suggestive for some pregnancy outcomes.

There were five studies -- sorry, six studies in the last five years, five of them on female exposures and one on male exposures. Of the five in maternal exposures, four were associated with some sort of effect, primarily miscarriage, or late spontaneous abortion, or preterm delivery.

In contrast, you know, other outcomes have been looked at. So there are two studies that looked at birth weight, none of -- neither of them found any effects on birth weight. There were two studies on neurodevelopmental effects that are suggestive. Female reproductive effects haven't really been evaluated in humans. There's only one study that did not observe any effects. And, you know, so I -- the animal evidence I didn't really take -- that wasn't sort of my charge, so I didn't really look in depth at the animal evidence. I think we'll hear from that next.

In terms of the human evidence, you know, there's some suggest -- some suggestive effects for pregnancy outcomes. And given the incredibly widespread use of this herbicide, you know, I initially ranked it as high.

CHAIRPERSON LUDERER: Thank you, Dr. Breton.

Dr. Plopper.

COMMITTEE MEMBER PLOPPER: Yes. Can you hear me

all right?

CHAIRPERSON LUDERER: Yes.

COMMITTEE MEMBER PLOPPER: I'm having trouble hearing you, so if you can hear me, that's great.

CHAIRPERSON LUDERER: Yes.

COMMITTEE MEMBER PLOPPER: My reaction is this would be a very high priority, because it is widely used. And just to follow-up on Dr. Breton's comments, the animal studies are extensive. And virtually all of them, whether they're looking at developmental impact, whether they're looking at reproduction, whether they're looking at impact on female reproductive organs, or male reproductive organs, or brain, particularly hippocampus, they all show that there are really significant effects.

And the other thing that I think should be concerning to the Committee is the fact that many of these effects for some of these long-term studies, they're looking at second and third generation animals after the exposure and they're finding even more serious effects. So I'd be glad to go into this in detail. There's 24 animal studies, four different species, and a wide variety of exposures strategies. So it's not like it's one particular exposure that's causing a problem. And the dose responses seem to be very -- show very strong impacts.

Every study that looked at sperm, as an example, all four of them, found exactly the same abnormalities and lasses. There's all -- I think there -- it could be considered a male toxicant, a female toxicant, and also probably a neurodevelopmental toxicant. So that's my comment.

CHAIRPERSON LUDERER: Thank you, Dr. Plopper.

Do we have any discussion from the Committee?

Dr. Woodruff.

COMMITTEE MEMBER WOODRUFF: Yes. Thank you. I just wanted to follow up briefly on the neurodevelopment, because that was a great summary by Dr. Plopper. I'll just note that the study, there is a epidemiological study. It's out of UCLA that's quite good in terms of how they did the evaluation of the exposures. And they looked across multiple pesticides. They didn't specifically start to look for glyphosate, but glyphosate came out as the -- and this was a study that looked at exposures to pesticides using California pesticide use data, but then including modeling of the data to make a -- to look at close to -- living close glyphosate use or other pesticide use and farther away.

And I thought what was very interesting about that study was even though they didn't start -- they did agnostically across all pesticides, glyphosate came up as

being significant continuously for the outcome of autism. So I think it's very interest --

COMMITTEE MEMBER PLOPPER: Yes.

COMMITTEE MEMBER WOODRUFF: -- I think it's very worthwhile for us to look at that, given the animal studies. And I just wanted to follow up and ask Dr. Plopper about this, because I know there's a number of study in bees finding neurodevelopmental effects in bees. Like they -- exposures can cause them to have difficulty in flying and other types of behavioral aspects. And I was wondering if you thought that if we did -- this did get prioritized, that that would be relevant literature to consider for this.

COMMITTEE MEMBER PLOPPER: Yes, I would. I was tying to avoid that issue, because it wasn't brought up here, but I think that is a major concern. And the other thing that I think is a concern about this is that the impact on the geese is a good example of why we need to consider this, because those geese are probably exposed buy aerosol, as well as by the water, as maybe by the food they eat.

And I hate to say this, but the way they are exposing, they are spraying this now everywhere, everyone is -- a large portion of the folks that are in agricultural areas are probably getting exposed. As

really of concern to me -- I was not going to bring it, but since you did, I will. The other -- the two things are the geese and the children. And the one thing that rather bothers me is that they now have limited the playgrounds for a distance close to a playground for children, but they haven't limited day care centers. And from the evidence we have from a experimental study, and Dr. Breton can comment on the epidemiology experimental studies, suggests that those first three or four years in children are when they're going to be most susceptible to this and the dose doesn't have to be very high.

Sorry, I didn't -- you got me into this. But the geese are the thing that got me concerned, but I thought I -- yes, I think you're right. And, in fact, that's a good example of nobody is doing anything. They're just watching these geese and it's causing a problem. Yes.

CHAIRPERSON LUDERER: All right. You were talking about bees, Dr. Woodruff, or...

COMMITTEE MEMBER WOODRUFF: Yes, I understand Dr. Plopper's comment went on --

(Laughter.)

COMMITTEE MEMBER WOODRUFF: Yes, the geese are also very interesting, yes (inaudible)

CHAIRPERSON LUDERER: All right. I just wanted to clarify that.

COMMITTEE MEMBER WOODRUFF: Right. But I do think it's interesting, because I mean we do have zebrafish studies in -- in the document, which I think is really important, because we typically only look at these mammalian studies. But I think that for some of these health effects, it's important to think more broadly, because effects can be observed across bees, so that was just --

CHAIRPERSON LUDERER: Right.

COMMITTEE MEMBER WOODRUFF: -- I wanted to make that additional comment.

CHAIRPERSON LUDERER: And certainly there was evidence from other non-mammalian species brought up for some of the other chemicals that we're reviewing today.

COMMITTEE MEMBER WOODRUFF: Right.

CHAIRPERSON LUDERER: Does anyone else in the panel have comments now before we turn to public comments? And then there will be more time for discussion after the public comments as well.

PUBLIC COMMENT

CHAIRPERSON LUDERER: All right. Then I know we have a number of public comments. I believe I have them all listed, but if I'm -- if I missed any, I'm sure that the staff will let me know. So we have Harvey Makishima, Public Awareness for Preventive Health Care, requested to

speak. And please limit yourselves to five minutes just as a reminder.

MEETING MODERATOR: Hi. Yes, I'm trying to unmute the individual, but I'm not sure where you're seeing their name -- their name listed.

CHAIRPERSON LUDERER: It's on my list oh -- it's on my agenda. So perhaps the agenda -- I mean we can move on to the --

DIRECTOR ZEISE: They did submit a card to speak, Jessica. You're not seeing them.

MEETING MODERATOR: Yeah, you said Harvey. I'm not seeing that anywhere.

DIRECTOR ZEISE: Harvey Makishima.

CHAIRPERSON LUDERER: Makishima, M-a-k-i-s-h-i-m-a, last name.

MEETING MODERATOR: No, I'm not seeing that. My apologies.

CHAIRPERSON LUDERER: We can move on to the next person. Maybe we can try to get that sorted out.

MEETING MODERATOR: Sure.

CHAIRPERSON LUDERER: All right. We have Zen Honeycutt from Moms Across America.

MEETING MODERATOR: All right. So I went ahead and unmuted you. You just have to unmute yourself on your end now.

MS. HONEYCUTT: Okay. Can you hear me?

MEETING MODERATOR: Yes.

CHAIRPERSON LUDERER: Yes.

MS. HONEYCUTT: Okay. Great. Thank you. Do you have my presentation?

MEETING MODERATOR: I do. Let me go ahead and pull that up now. Give me one second.

MS. HONEYCUTT: Okay. Great. While that's coming up, I just want to thank all of you for taking the time to do such a thorough, you know, investigation of these different chemicals. As a mom who has been focused on glyphosate for eight years of my life now, you -- like, you're my heroes. Thank you so much for taking the time to review this and all of the other chemicals, which I don't have the time to. I have not taken the time to review, so I appreciate you looking at all the other chemicals as well.

MEETING MODERATOR: All right. You should see your presentation now.

(Thereupon a slide presentation.)

MS. HONEYCUTT: Oh. Okay. Great. So you can go ahead to the next slide.

NEXT SLIDE

MS. HONEYCUTT: I'm Zen Honeycutt from Moms Across America. We're a non-profit and we're asking you

to please lift prop -- glyphosate herbicides on the Prop 65 list or put it as a high priority. I would put it first priority considering the amount of use for all of these different reasons and I'm sure you'll see many more as well.

Next slide.

NEXT SLIDE

MS. HONEYCUTT: First, I want to point out that glyphosate is never used alone and therefore we request that you review the studies that include the glyphosate full formulation and base your decision whether or not to list glyphosate on the California Prop 65 list as a reproductive effect or endocrine disruptor, based on studies that also include the full formulation.

Next slide.

NEXT SLIDE

MS. HONEYCUTT: And I'd like you to -- my request is that you also consider all of the different areas in which glyphosate can impact the endocrine system, not just the reproductive organs, you know, including, as one of the previous speakers mentioned, the brain, also the thyroid, the kidney, the heart, the pancreas, the testes. And my presentation we have studies here linked to -- we have links to studies in the words that are in blue, like the thyroid, and the liver, and breast de -- birth

defects, and breast, and autism issues, and also developmental delays.

Next slide.

NEXT SLIDE

MS. HONEYCUTT: One, in particular, paper to look at is the Munoz et al. paper, which actually shows nine different pathways in which glyphosate does impact the endocrine system sand hormone receptors. And I appreciate you taking a -- you know, giving that paper your concerted attention.

Next slide.

NEXT SLIDE

MS. HONEYCUTT: I'd like to point out that endocrine disruptors can cause, you know, the birth defects, miscarriages, preterm births, developmental delays and death. And there is the three studies that show they are toxic to human placental cells. Studies -- both in -- I just mentioned France here, but there's also Argentina and many other places, especially in Washington, regarding anencephaly, where there's birth defects shown after families have been exposed to pesticides, particularly glyphosate herbicides.

And also, there's a higher risk of birth defects in live births with exposure to agrochemicals in particularly glyphosate in surface water.

Next slide.

NEXT SLIDE

MS. HONEYCUTT: Glyphosate has been shown to be an endocrine disruptor in numerous animals, as Dr. Plopper mentioned. Also, I'd like to include rabbits, amphibians, and pigs. And the pig study is very interesting out of Denmark, because he had thousands of pigs and when he sprayed them the non-glyphosate -- fed them the non-glyphosate sprayed greens, they had three percent of birth defects. When he gave them the glyphosate-sprayed greens, it went up to 33 percent of the sows had birth defects. So that's a very interesting one to look at.

Next slide.

NEXT SLIDE

MS. HONEYCUTT: Also, I'm sorry about the slide here. The EPA has just recently found and has -- just found that glyphosate harms endangered species. It's 93 percent of the species and 97 percent of the critical habitats, that's 1,676 species. And what's interesting is that they also found that it's moderately toxic to mammals. And the last time I checked, our children and we are ani -- mammals. So your consideration greatly impacts our current and future generations as well. And one of the primary ways that glyphosate harmed this species is by endocrine disruption.

Next slide.

NEXT SLIDE

MS. HONEYCUTT: Please consider that glyphosate is sprayed as a drying agent on crops such as wheat, and that impacts the farming communities. And also, I'd like to mention there's another study that just came out that shows epigenetic effects by Maamar, M-a-a-m-a-r. It just came out today and it actually shows third and fourth generation increase of diseases by when the males were exposed to glyphosate and that was an animal study, a rat study. So that's a brand new one that came out today.

Next slide.

NEXT SLIDE

MS. HONEYCUTT: The runoff into waterways comes from agriculture and landscape use. It's 285 million pounds per year is used in the United States. And one study shows that 71 pregnant women had a significantly correlated with glyphosate exposure with shortened gestational lengths, which we all know means miscarriages, infertility and infant death, which, of course, is tragic. And glyphosate has been detected in human breast milk, dairy, eggs, and thousands of food -- U.S. food samples. So we're being exposed to it every day.

Next slide.

NEXT SLIDE

MS. HONEYCUTT: The American women are also experiencing a rise in infertility. This is old data, but you can see the rise. And please keep in mind that assisted reproductive technologies are only really for the wealthy people. So this is -- this data doesn't even though that -- you know, a bit of the impact of our infertility problem that we have in America.

Next Slide.

NEXT SLIDE

CHAIRPERSON LUDERER: Ms. Honeycutt, I think Dr. Zeise is trying to get our attention, because you've used up your five minute time. Could you please wrap it up for us?

MS. HONEYCUTT: Okay. Yeah, sure.

CHAIRPERSON LUDERER: Thank you.

MS. HONEYCUTT: You can just go through the next slides --

NEXT SLIDE

MS. HONEYCUTT: -- just to cancer. And the next slide. Sorry about that.

NEXT SLIDE

MS. HONEYCUTT: And then thyroid issues.

NEXT SLIDE

MS. HONEYCUTT: And then, of course, this one that shows that it causes autism effects and liver

disease.

And then I just have a list of the studies. Thank you so much for your time. I appreciate it.

CHAIRPERSON LUDERER: Thank you very much for comment.

Were we able to find Harvey Makishima? Is that person available to comment at this point, Jessica?

MEETING MODERATOR: Let's see. I am going through the list again. Yeah, still not -- still not seeing it.

CHAIRPERSON LUDERER: Okay. If not, we can move on to the -- and you can just please let me know if after the next group of people is finished whether that person has arrived.

MEETING MODERATOR: Absolutely.

CHAIRPERSON LUDERER: So the next, we have three commenters from Bayer Crop Science, the -- Donna Farmer, Steven Levine, and John Acquavella. I'm not sure which order, if that's the order they're planning on presenting in.

Donna Farmer is listed first here.

MEETING MODERATOR: I will go ahead with Donna. Donna, I'm going to go ahead and unmute you and you should be able to hear us and speak now.

DR. FARMER: Can you hear me?

MEETING MODERATOR: Yes.

CHAIRPERSON LUDERER: Yes.

DR. FARMER: So I will go first, followed by Dr. Levine and then Dr. Acquavella.

(Thereupon a slide presentation.)

DR. FARMER: Good morning or good afternoon, I think we're right at your lunchtime. On behalf of Bayer Crop Science, I would like to thank OEHHA, and the Chair, and the members of the DARTIC for the opportunity to speak to you today about glyphosate and its salts. I'm Donna Farmer. I'm a Senior Science Fellow in Bayer's Regulatory Human Safety Center. And I have provided toxicology support for glyphosate over 20 years. I have a PhD in anatomy and cell biology from the University of Cincinnati College of Medicine. And prior to joining the company, I held faculty positions in departments of anatomy like Dr. Plopper, and also in obstetrics and gynecology.

And I really appreciate how difficult this task is and the hundreds of publications that are out, both on glyphosate and on the glyphosate formulations. But another thing that I want to bring your attention to is that, you know, normally as pesticide we have to be regulated. And normally, there's one regulatory data package that's enough to assess endpoints relative to human health, but in this unique case, there are seven.

When glyphosate went of patent, other manufacturers of glyphosate developed and submitted their own data packages to regulatory agencies around the world. And the results of those studies are remarkably consistent and agencies have concluded that glyphosate is not a reproductive or developmental toxicant, and is not an endocrine disruptor. And they also take into consideration the published literature.

Glyphosate is highly regulated. It's toxicology is well understood and accordingly, it should be lower priority for future review, in our opinion, for Prop 65.

Now, included in those regulatory data packages, or toxicology studies, they specifically evaluate reproduction and development. And for glyphosate there are 10 rat multi-gen reproduction, 15 rat and rabbit developmental toxicities. In addition, many of other required studies listed as subchronic and chronic, including neurotoxicity, have endpoints that also will be informative on male and reproductive systems.

Now, these regulatory studies must be conducted according to accepted guidelines as indicated on slide 2. And on the list of 24 animal studies provided to DARTIC, only two regulatory studies, a rat developmental toxicity and rabbit chronic onco study were included.

Go to slide 2, please.

NEXT SLIDE

DR. FARMER: Fifteen of those 24 studies report findings -- of those 24 studies that were listed for DARTIC, 15 of those report findings only after an exposure to a glyphosate-based formulation. And we're talking about glyphosate today. And we'd be happy to talk about the formulations at another time, but these studies were conducted in seven different countries, using seven different formulations, and have really limited value in determining if glyphosate is a reproductive or developmental toxicant. And again, we'd be happy to discuss formulations at a later date.

In terms of the -- I'm going to focus -- I'd like to briefly on the next slide --

NEXT SLIDE

DR. FARMER: -- discuss the design and data collected from a multi-gen reproduction study. The multi-gen reproduction study, of which there are 10 for glyphosate, this is a very large study with many endpoints. It is designed to provide information concerning the effects of the test substance on the integrity and performance of the male and female reproductive systems throughout successive generations.

Considering all the available multi-generation studies on glyphosate, glyphosate was concluded not to be

a reproductive toxicant. And the overall multi-generational no-observed-adverse-effect-level, or the NOAEL, in rats for parental offspring -- parental offspring and reproductive toxicity is 700 milligrams, per kilogram, per body weight, per day.

And the next slide --

NEXT SLIDE

DR. FARMER: -- to put that multi-generational NOAEL in perspective, and a lot of you have been talking (inaudible) so use doesn't always equate to exposure and exposure doesn't always equate to a high internal exposure.

I call your attention to the green box and the arrow. On logarithmic scale, that NOAEL, where no effects were observed, is six to eight orders of magnitude higher than glyphosate levels from bystanders in the general population. And the applicator exposure is in the similar range. And Dr. Acquavella has published on applicator of exposure and I assume he will provide further comment.

Now, going back to that list of 24 animal studies that Dr. Plopper mentioned, seven of the published studies were conducted with glyphosate, five were in rats and two were in mice.

In evaluating those studies, there was an inconsistency in the study design, the number of animals,

the duration and route of exposure. It went from a biscuit, to an intraperitoneal injection, to water exposure. Difference in the endpoints that were assessed, and there was a lack of consistency in results between the studies. So some studies had effects on testes, others didn't. So had effects on ovaries, others didn't, and had an effect on anogenital distance, others didn't.

Overall, these studies do not provide complicit evidence that glyphosate adversely affects reproduction or development.

In conclusion, regulatory authorities around the world reviewed the multiple regulatory data packages and the published literature in a weight-of-evidence evaluation and have concluded that glyphosate is not a reproductive or developmental toxicant and is not an endocrine disruptor.

Again, glyphosate is highly regulated, its toxicology is well understood, and accordingly, it should be a lower priority for future review into Proposition 65.

I again thank you for this opportunity to speak and I'd be pleased to answer any questions from the Committee.

CHAIRPERSON LUDERER: Thank you, Dr. Farmer.

I think we're -- we'll move on to Dr. Levine.

MEETING MODERATOR: All right, Dr. Levine, I'm

going to go ahead and unmute you. You have to go ahead and do it on your end. And I will go ahead and pull up your slides as well.

DR. LEVINE: Thank you. Thank you. I'll wait till you pull up the slides.

MEETING MODERATOR: All right. I am just moving them over. It should take a few seconds. All right. Perfect. Let me show my screen.

Okay. You should be seeing them now.

(Thereupon a slide presentation.)

DR. LEVINE: Okay. Thank you. Good afternoon, everyone. I'm Steve Levine. I'm an environmental toxicologist and a Bayer Distinguished Fellow. And what I'm going to talk about today are mechanistic studies with glyphosate that further inform the developmental and reproductive toxicity assessment. And this will build on the information you've just heard.

Next slide, please.

NEXT SLIDE

DR. LEVINE: In 2010, glyphosate was screened for its potential to interact with the estrogen, androgen, thyroid, and steroidogenic, or EATS, pathways under EPA's Endocrine Disruptor Screening Program, or the EDSP.

Glyphosate was not selected based on known or likely endocrine activity and was only tested because it

met qualitative criteria, human exposure. Glyphosate was screened in all 11 EDSP validated assays following GLP, and the list of studies is to the right. And I'll elaborate on those on the next slide. The majority of these assays had mechanistic endpoints and several assays also had apical endpoints that assessed the hypothalamic, pituitary, gonadal, and thyroid axes for potential developmental and reproductive effects. All of these assays were accepted as valid studies by EPA and used in a weight-of-evidence analysis.

Next slide, please.

NEXT SLIDE

DR. LEVINE: This table summarizes the EDSP data and it showed no interaction with the endocrine system and "NI" in the cells below denotes no interaction. If you look on the left-hand side, those are the 11 screening assays, five in vitro mechanistic assays and six in vivo assays. The in vivo assays provided mechanistic information, as well as looking at apical endpoints, such as reproduction and development.

If you look across the top, the row on the top, it looks at the different modes of action that were investigated, estrogenicity, anti-estrogenicity, androgenicity, anti-androgenicity, as well as steroidogenesis, so effects on testosterone and estrogen

levels, as well as potential integrated effects on the hypothalamus, pituitary, gonadal, and thyroid axes.

The strength of this battery is its redundancy. And if you look down, for example, to the column for estrogenicity, you'll see that multiple assays interrogated that mode of action, okay, not only for estrogenic mechanistic assays, but also, for example, for steroidogenesis.

The strength of looking at this in the context of a weight of evidence is this really looked at multiple different levels of biological organizations, all the way from the subcellular level, such as receptor binding, gene activation, the organ level and the uterotrophic assay, development in the pubertal assay and reproduction in a short-term fish reproduction assay. And again, this data lends itself very well to weight of evidence. And no activity was observed for any of these different modes of action across the battery.

Next slide, please.

NEXT SLIDE

DR. LEVINE: EPA evaluated this battery in 2015 and EFSA had done the same thing in 2017. And beyond the EDSP data, they brought in all other scientifically relevant information. That included toxicology studies that had endpoints that had formed and endocrine

assessment, as well as the relevant and reliable information in the peer-reviewed literature based on their systematic review. And based on their evaluations, they concluded that estro -- that the estrogenic, androgenic, and thyroid pathways, including steroidogenesis are not impacted by glyphosate.

So in closing, the results from the EDSP further support the results from the comprehensive regulatory toxicology database ensuring that glyphosate is not a reproductive or developmental toxicant.

Because I heard something about geese or birds, I just want to point out that there are multiple avian reproduction studies and glyphosate has shown no impact on reproduction in avian species and there's also been extensive regulatory testing in the area for bees, looking at potential effects on larval and adults. Many of those studies that have been used for regulatory purposes have been published. And I would point you to those in the literature. So I'm going to stop there and see if there's any questions.

Thank you.

CHAIRPERSON LUDERER: Thank you, Dr. Levine. I think we'll go on to the third presentation and then if there are any questions from panel members, perhaps all three of you could answer at the end.

The next speaker then is the Dr. Acquavella. And, Jessica, can you unmute him, please?

MEETING MODERATOR: Yes, let's see. Find the name on the list. And also, I haven't seen -- Harvey never -- I never saw that name listed either, so apologies there.

CHAIRPERSON LUDERER: All right.

MEETING MODERATOR: Let's see here. One more time, give me the name here. I'm not seeing it listed. John Acquavella, A-c-q-u-a --

MEETING MODERATOR: Oh, here we go. Perfect. Okay. John, I'm going to go ahead and unmute you. You will still be self-muted, so just make sure you click the button again as well. All right. You can go ahead and speak. We should be able to hear you now.

CHAIRPERSON LUDERER: Is there a presentation?

MEETING MODERATOR: Yes, I'm pulling that up next.

(Thereupon a slide presentation.)

MEETING MODERATOR: All right. John, you are unmuted, so you should be able to speak. And you should see your presentation as well.

We're not hearing you.

MEETING MODERATOR: John, if you need to -- I don't know if you can hear me, but if you go up to your

control panel where it says audio, it shows that you're using computer audio, which is unmuted. If you briefly click over to either whether it says no audio or to the phone audio, let it sit there for a few seconds, and then toggle back over. Okay. It looks like he's switching his audio now.

All right. I just unmuted you again, go ahead and -- yeah, see if you can speak now.

CHAIRPERSON LUDERER: We're not hearing him.

MEETING MODERATOR: All right. John, if you can still hear me, go ahead and toggle back over to the phone and let's have you dial in, because we're not getting any audio. And then once his phone turns green, I'll be able to -- to unmute him again. Now, John, you are connected via phone now. If you can go ahead and enter in that PIN number that I'm sending you, you'll be able to unmute yourself.

All right. John, you're unmuted again. Go ahead and speak for us.

CHAIRPERSON LUDERER: We still don't hear anything.

MEETING MODERATOR: Yeah, he's actually reaching out in the questions pane. So I'm going to see if I can text him what to -- what to do next. I'm going to go ahead and mute myself briefly.

Okay. John, I just sent you a response in the questions pane. If you can hear me, what I put in there is if you go to the audio pane again, your microphone is it on. But GoToWebinar might have it set to maybe the computer audio, where it's using that speaker. So if you can look at that dropdown in the microphone section, see if you have more than two options and switch through -- through the options that you have there and we'll see if we can hear you.

CHAIRPERSON LUDERER: Yeah, we're still not hearing anything.

MEETING MODERATOR: Okay. John, I unmuted you again. Go ahead and see if you can speak now.

CHAIRPERSON LUDERER: Jessica, would it possible for you to maybe try to continue troubleshooting while we call on the next person who requested public comment?

MEETING MODERATOR: Sure. Yeah. Absolutely. I'm writing him in the background, but, yeah, who would you like to -- to go next.

CHAIRPERSON LUDERER: I think -- I think the last person that I have on my list, and some from the staff can correct me if I'm wrong, is Jennifer Sass from National -- Natural Resources Defense Council.

MEETING MODERATOR: I do see Jennifer here. All right, Jennifer, I'm going to go ahead -- you are

self-muted. I unmuted you on my end. Go ahead and click the button again. You should be able to speak.

CHAIRPERSON LUDERER: And did -- are there any slides?

MR. LEICHTY: No slides.

MEETING MODERATOR: Yeah, I don't believe so. Okay.

CHAIRPERSON LUDERER: Okay.

DR. ACQUAVELLA: Excuse me. Can you hear me now?

MEETING MODERATOR: Yes, we can.

CHAIRPERSON LUDERER: Is that Dr. Acquavella?

DR. ACQUAVELLA: Oh, terrific. Thank you. Okay. So I'll wait and speak after or I'll speak now as you prefer.

CHAIRPERSON LUDERER: Well, since your slides are up and we are waiting for you, why don't you go ahead and then we'll proceed with Dr. Sass.

DR. ACQUAVELLA: Okay. Great. Thank you. I'm a professor of clinical epidemiology at Aarhus University in Denmark, but I have a history with glyphosate epidemiology and biomonitoring.

So next slide.

NEXT SLIDE

DR. ACQUAVELLA: What I thought I'd do is share some biomonitoring results that I think are informative

with regard to the exposure metrics used in epidemiology studies.

Next.

NEXT SLIDE

DR. ACQUAVELLA: And I'm going to speak mainly from the farm family exposure study where we biomonitored farmers and their families for 24 hours before, 24 hours the day of, and for three days after applications on their farm for either glyphosate, 2,4-D, or chlorpyrifos.

Next slide.

NEXT SLIDE

DR. ACQUAVELLA: So the direct exposure scenario is represented by the applicators. You can see for glyphosate 60 percent had detectable values. We monitored these chemicals in urine with a one part per billion limit of detection. Forty percent of the farmers actually didn't show detectable glyphosate, including nine who did applications of 100 acres or more. The average application size was 90 acres, so this was quite different than for the other chemicals.

Next slide.

NEXT SLIDE

DR. ACQUAVELLA: If we plot the geometric mean values by day of study, you can see glyphosate is excreted rapidly, that's the green curve, consistent with the

consensus half-life of 6 to 12 hours.

And next slide, please.

NEXT SLIDE

DR. ACQUAVELLA: This is the cumulative dose distribution. And you can see that all the glyphosate values, again the green curve, are clustered around the median, which is 10 to the minus 4th milligrams per kilogram, with just a few values that went up to about 10 to the minus third milligram per kilogram.

Next slide.

NEXT SLIDE

DR. ACQUAVELLA: Now, the spouses in this study, none of whom mixed or applied glyphosate, provide insight into the indirect exposure scenario. And only two of the 48 spouses actually had detectable glyphosate in their urine as a result of an application on their farm.

Next slide.

NEXT SLIDE

DR. ACQUAVELLA: The children provide information about both the direct and indirect exposure. Some of the children worked with their father on this application. And they had a profile that looked just like the applicators, but 52 children didn't work on the application, and only one of the 52 had a measurable level of glyphosate in the urine.

Next slide.

NEXT SLIDE

DR. ACQUAVELLA: So in conclusion, we have a pretty good handle on direct glyphosate exposure scenarios. The doses tend to cluster around 10 to the minus 4th milligram per kilogram versus the NOAEL that Dr. Farmer mentioned. The indirect exposure scenarios were predominantly less than the limit of detection, reflecting minimal internalized dose for residents on the farm where glyphosate was applied.

And so I know a number of the epidemiology studies used remote exposure metrics. I just don't see how they can be valid when we can't even measure glyphosate in the urine of people who are living on the farms where the applications were made. And I think before those remote metrics can be taken at face value, some validation needs to be done.

Thank you.

CHAIRPERSON LUDERER: Thank you, Dr. Acquavella.

Are there any questions from the panel for speakers so far?

Okay. Then we will move on to Dr. Sass from NRDC. And I think you said there were -- there are no slides for that talk, is that right, Jessica?

MEETING MODERATOR: Correct. Let me go back and

on unmute. Let's see here. All right. So you should be able to unmute yourself now and be able to speak.

Jennifer, if you can hear me, if you go over to where your name is listed, there's going to be a red microphone next to your same. Go ahead and click on the red microphone and it will unmute you on your end.

COMMITTEE MEMBER BASKIN: Am I the only one that our last speaker kind of cut out at his summary statement?

CHAIRPERSON LUDERER: Yeah, I didn't have that problem. Did anyone else have it?

(Heads shake.)

CHAIRPERSON LUDERER: No.

COMMITTEE MEMBER BASKIN: Sorry.

MEETING MODERATOR: I'm going to send Jennifer a message just in case she cannot hear me. Let me see.

(Multiple voices.)

MEETING MODERATOR: So sorry, what was that?

DIRECTOR ZEISE: I just -- while you're sorting that out, I do think there's one more speaker card from Gary Roberts. So while you sort that out, you may want to take -- Ulrike, you might want to take --

CHAIRPERSON LUDERER: Okay.

DIRECTOR ZEISE: -- Gary Roberts and then Jennifer Sass.

CHAIRPERSON LUDERER: Okay. Jessica, do you --

can you unmute Gary Roberts?

MEETING MODERATOR: Yes. I see him right here.

CHAIRPERSON LUDERER: Okay.

MEETING MODERATOR: All right, Gary, I'm going to go ahead and unmute you from my end. You should be able to click the button and be unmuted.

MR. ROBERTS: Can you all hear me?

MEETING MODERATOR: Yes.

CHAIRPERSON LUDERER: Yes.

MR. ROBERTS: Excellent. Thank you for your time. I'll be brief. On behalf of Bayer, I offer this comment concerning glyphosate and a chemical you'll consider later and imidacloprid.

Each of these two chemicals, you've been presented with written scientific evidence that U.S. EPA, an authoritative body, has recently examined all Prop 65 relevant aspects of the reproductive toxicity of these chemicals, developmental, male and female.

For glyphosate, you were presented with a conclusion from U.S. EPA in the Bayer comments that was reaffirmed less than two months ago, was originally announced in January 2020, and that says there are quote, "No risks of concern to human health from current uses of glyphosate," closed quote. Of course, this includes a determination of no concern for reproductive toxicity.

For imidacloprid, the human health draft risk assessment for registration review offered a similarly reassuring discussion at pages 14 to 15 of the document, which was noted in Bayer's comments. These EPA assessments fall within a specific provision of your prioritization procedure that I want to underscore.

The prioritization procedure, part of your materials and referenced earlier by OEHHA staff, in the third full paragraph on page four says quote, "It is unlikely that chemicals will be proposed for DART Identification Committee review that have been recently reviewed by an authoritative body and found to have insufficient evidence of reproductive toxicity". Cancer references were emitted from that quote.

EPA has determined there is insufficient evidence of reproductive toxicity chemicals. Further, there is no reason for the Committee to depart from its normal practice of placing chemicals such as these in a lower priority ranking.

And this makes sense. These chemicals have been recently reviewed by a body that this Committee specifically considers authoritative. Moreover, you have heard and will hear that the weight of the evidence strongly supports EPA's assessments. And EPA does not stand alone. Regulators all over the world agree. In the

case of glyphosate, for example Brazil, just drew the same conclusion earlier this month.

I would be pleased to answer any questions you may have. Thank you.

If there are no questions, I'll reserve the remainder of my time.

CHAIRPERSON LUDERER: Thank you very much, Dr. Roberts.

And our last commenter is Dr. Jennifer Sass. Are we able to get audio for her?

DR. SASS: Yes. Can you hear me now?

CHAIRPERSON LUDERER: Yes.

DR. SASS: Yeah. Thanks. I can see you nodding your heads. I apologize. I was thwarted by having multiple screens and multiple documents and I undermined my ability to navigate it.

So therefore, I'm going to actually just give very short comments on this one. I am going to also comment on the neonicotinoids, which are coming up in the next discussion. But for this one, I'll only direct you to my written comments on glyphosate and to say that we at NRDC, the Natural Resources Defense Council, strongly support moving this nomination further. We're very concerned about the human health impacts of this and we -- I refer you to my details in my comments, as well as the

document that the staff put together, which is very good, and some of the previous commenters. So thank you.

COMMITTEE DISCUSSION AND RECOMMENDATION

CHAIRPERSON LUDERER: Do we have any other discussion by the Committee or questions?

Dr. Allard.

COMMITTEE MEMBER ALLARD: Yeah. I guess maybe I can just like think out loud here about the process in my mind. The fact that glyphosate is one of the -- if not the, I think, most prevalently used herbicide and that its use is going to increase or has already increased absolutely dramatically over the last years in California, in the U.S., and in the world, and, you know, balancing the need to perhaps look further at a chemical that perhaps is not -- does not have overwhelming evidence from all fronts or as has been reviewed by other entities, but, yet, is it our duty -- perhaps, it is our duty -- at least in my mind, it is our duty to provide an independent review of other organizations to make sure that something that is as prevalently used in California, and in many other places, is indeed safe.

So that's -- so that's the things that I'm balancing here, you know, the public health aspect versus the data and balancing these two aspects. So, I mean, I'll be voting, so I'll -- people will know where I stand

on that, but I -- you know, that's sort of -- we cannot just look at the data. We also have to look at the incredible use of this chemical in California.

CHAIRPERSON LUDERER: Dr. Woodruff.

COMMITTEE MEMBER WOODRUFF: Yeah. I just wanted to follow up on the issue about the increasing use, because I know we didn't -- I'm not sure it was covered in here. But there was a study published -- there's been several studies published on the increasing use of glyphosate or prevalence of it over time. And there was a study in JAMA that looked at levels in people from the nineties to more recently, and the amount of glyphosate they measured in the people has gone up dramatically. And it's higher -- I'm going to try and look at this, is -- it's -- they measured it in a significant portion of people.

So I feel that even though we may have not had so many measurements of glyphosate in the past, that we're going to be seeing higher prevalence of that -- of people in the -- higher amounts of glyphosate in people. And I also wanted to comment that a lot of the regulatory bodies that -- the regulatory bodies look at glyphosate slightly different around the world. Some of them look just at hazard, like we are charged to do. We're -- is my understanding. Correct me if I'm wrong, from the OEHHA

staff, is that we only look at hazard. We don't consider the exposure levels. A lot of the other regulatory bodies that look at -- have made pronouncements about glyphosate incorporate both hazard and exposures. So I think that's an important distinction.

CHAIRPERSON LUDERER: Thank you, Dr. Woodruff.

I had Dr. Pessah, you had your hand raised and -- yeah, go ahead.

COMMITTEE MEMBER PESSAH: Yeah. Actually, I have a question for those that actually reviewed this extensively. You know, it's a very important question of what the trends are going to be like with exposure. And what I hear is that there's quite a discrepancy between current levels of exposure, even for most highly exposed, and the concentrations and/or the doses used to produce effects in animals. And I wonder if that's an order of magnitude, five orders of magnitude. Where are we with that, because that has a real impact on potential risk?

CHAIRPERSON LUDERER: Dr. Plopper, did you have a comment?

COMMITTEE MEMBER PLOPPER: That's a very good question. And the problem that I have is that the way these -- we would need to do a thorough analysis, because the way these are administered, or where they're taken in and have a very different impact. And one of the problems

with these studies, which I didn't think we had time to go into now, is that there are different formulations used. And the formulations I think Dr. Woodruff made a very good point. It's using more, but if you look at the formulations that were used 10 years ago, I suspect my brief look was that they're different. And they run all the way from less than one percent of the chemical is -- is glyphosphate[SIC] up to almost a hundred percent. And the other additives are generally used to promote introduction of this chemical into whatever it's being sprayed on. And that could be -- also be people.

So I think those are major concerns. And the problem is that there -- the studies are -- like Dr. Woodruff said, the studies are getting better and more relevant as to what the current concentrations are in people. And I think that's what we would need to look at. And I don't think it's a simple question. It's a very complex one.

But it does concern me that some of these experimental studies talk about more than one generation after the exposure of finding negative effects. And that would what -- concern me as much as anything is that whatever -- it may not be an effect that has an impact on a pregnant mother for instance, but it may on her grandchildren. And there's already experimental evidence

that would suggest that's true.

So I don't know what to say. I think just my personal opinion is that there's so much of this chemical used in California, that the -- it would be irresponsible not to take another look because, as Dr. Woodruff said, we do this in a different perspective than a lot of these other regulatory agencies.

So I don't know if that's answered your question, but it's a pretty complicated issue, because there's so much of it and its composition -- chemical composition is very different.

COMMITTEE MEMBER PESSAH: Thank you. That was very helpful.

CHAIRPERSON LUDERER: Thank you.

Dr. Hertz-Picciotto.

COMMITTEE MEMBER HERTZ-PICCIOTTO: I just want to speak to, you know, emerging evidence and I noticed that this paper was not -- not in the document. It came out in I think it's 2018. It's Shrestha and this is a study using this very large Agricultural Health Study supported by the national institutes of health. It's been going on for over 20 or 30 years now. And it has about 37,000 people who are part of the study.

And this was a study where they look at hypothyroidism. And there were -- there's actually very

strong evidence in this paper of hypothyroidism. But actually there's a table -- of course, they were looking at many, many pesticides. And the number of exposed cases to glyphosate is larger than any of the other -- no, no. There's one more -- there's one other. 2,4-D is actually just slightly higher with 671. But there were 663 cases and this have -- did have an elevated and significant relative risk or -- in this study that was quite significant.

And the -- it's -- it's a well-known study, you know, authors who have been working on the Agricultural Health Study for many, many years. So I think this is -- this -- this is one of those outcomes that is certainly of great significance for reproductive and developmental harm. And I think, you know, some of -- there are new studies coming out all the time, so it's possible that other agencies can reach other conclusions looking at different data -- you know, the date that Dr. Acquavella presented was from, I think, 2004 and 2006, as far as exposure.

So whether those exposures are still relevant to today's populations in the -- agri -- for agricultural uses might be something to question.

CHAIRPERSON LUDERER: Great. Thank you very much. I don't see any other hands raised. And I don't

believe we have any additional public comments. So then we can move on to our Committee recommendation. So again, I'll go through the high, medium, and no priority. And please raise your hands and I'll call the names of all the hands that I see.

So who recommends that this be place on high priority, please raise your hands.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Woodruff, Dr. Plopper, Dr. Auyeung-Kim, Dr. Baskin, Dr. Pessah, Dr. Carmichael, Dr. Breton, Dr. Picciotto, and Dr. Luderer.

And then who -- I think we have one person who hasn't voted yet. Medium?

(Hand raised.)

CHAIRPERSON LUDERER: Dr. Allard votes for medium priority. Okay. All right. Thank you, everyone.

I think it's time now to break for lunch. So we have a 40-minute -- 40 minutes allotted to lunch. It's about 12:45. So shall we say then that we meet at -- let's say, what did we say? Forty -- we had 40 minutes. So 1:55?

COMMITTEE MEMBER ALLARD: Can I ask about --

CHAIRPERSON LUDERER: So 1:25, sorry. Yes.

COMMITTEE MEMBER ALLARD: Can I ask about timing for the rest of the day, because we are at -- I don't

think we've hit half of the chemicals that we're supposed to discuss today, right, so --

CHAIRPERSON LUDERER: Well, we're actually exactly where we were on the schedule, which was that we would break for lunch --

COMMITTEE MEMBER ALLARD: Okay.

CHAIRPERSON LUDERER: -- around 12:45 to, yeah, 12:30 to 12:45, so it's 12:45 now.

COMMITTEE MEMBER ALLARD: Okay.

CHAIRPERSON LUDERER: So we're actually doing pretty well.

COMMITTEE MEMBER ALLARD: Great.

CHAIRPERSON LUDERER: Yes.

DIRECTOR ZEISE: So 45 minutes would be -- did you say 1:35 or sorry 1:25, ulrike?

CHAIRPERSON LUDERER: 1:25, yeah, is that good? Is that what you're proposing.

DIRECTOR ZEISE: I think that would be --

CHAIRPERSON LUDERER: Okay.

DIRECTOR ZEISE: -- that would be okay.

CHAIRPERSON LUDERER: Okay. All right. Okay. So 1:25 we'll see everyone back.

(Off record: 12:45 p.m.)

(Thereupon a lunch break was taken.)

AFTERNOON SESSION

(On record: 1:25 p.m.)

MANGANESE

COMMITTEE DISCUSSION

CHAIRPERSON LUDERER: All right. I think the Committee is here, so I think we can reconvene and get started with the afternoon part of our meeting.

So our next chemical under consideration is manganese. And the lead discussants for that are Dr. Pessah and Dr. Hertz-Picciotto.

Dr. Pessah, would you like to start?

COMMITTEE MEMBER PESSAH: Can you hear me now?

CHAIRPERSON LUDERER: Yes.

COMMITTEE MEMBER PESSAH: Okay. So manganese is both an essential element and a potent toxicant. And the reason for that is manganese takes part in many enzymatic reactions in the body, both in the central nervous system and out in the periphery, so it's tightly regulated. And sources of manganese include occupational exposure, particularly miners and welders that can have high levels.

In fact, acute effects are essentially termed manganism. But more recently there have been low level effects that are relevant to developmental and neurotoxicity. And these include disruption of the hypothalamic axis that disrupt gonadotropin releasing

hormone and luteinizing hormone. These effects have been shown to impact both the reproductive success and reproductive outcomes, as well as puberty and sex hormone outcomes in offspring.

There have been several studies published within the last year that indicate both reproductive and in developmental outcomes with both chronic exposure as well as low level chronic exposure. I think these outcomes have been, to some extent, seen in human studies, but I'll let Dr. Hertz-Picciotto comment on these.

So I would have -- I rank it in a high relevance category.

COMMITTEE MEMBER HERTZ-PICCIOTTO: Okay. So I guess I'm going to start by saying there really are, I think, these two issues. You know, one is what is the evidence around high exposures to manganese and this issue, because it's an essential element, you know, at low levels, deficiencies will cause some of the same actual adverse outcomes as high levels to me.

So there are a number of studies in showing this inverted U shape or depending on how you get the -- you know, so the optimal is in that middle ground, middle area of exposure and -- or dose. And that I think this is going to be really a discussion we have to have about the idea of listing something. And on the one hand, I

think -- and I can -- I'll talk through some of the outcomes, but really quickly in a moment.

But basically, the bottom line is reproductive outcomes, an abundant literature, birth weight particularly, and other outcomes, neurodevelopment as well, and then the endocrine and reproductive impacts.

So what -- you know, that's one part of the story. But the other part is then do we want to have labeling that says, you know, this product contains manganese, which is known by the State of California to cause birth defects and other developmental harm, or whatever the -- I think that's about the language. And so my concern really is about Prop 65, its process, and what -- would there be some way to modify the messages that -- or is that part of the statute itself or regulation where -- so I just be -- I feel like this is really a critical issue and I -- and I don't know how much of this is OEHHA's job to sort that out versus us as this Committee.

Again, I think at the high doses that are relevant, but not high, like astronomically high. I'm just -- at the high levels that are seen in these epidemiologic studies, there -- there is very clear harm. And this is -- this is a huge literature -- I mean, there were 50 or so papers, and the vast majority of them were

seeing harmful effects at the high end. Some of the studies were in populations where their entire range is kind of at the high end.

So they would see linear effects. And then some were all kind of below end that we're seeing linear in kind of the other direction, where higher was -- was better, if you're down in the low range, so -- but then a lot of that, I think, was resolved by looking at the range of those exposures. And you do see these U-shaped and inverted U, depending on whether your XY axis is a benefit or a harm.

And so -- so that's, to me, I feel like the crux of what we do here really depends on how -- how can we -- is there a way to adapt the Prop 65 process and mission for some -- for a chemical that really does have critical benefits at the low dose -- you know, so that deficiency is not what we want to see people ending up with at the end of the day.

And then just to talk through, you know, we've got birth weight, we've got birth length, we've got Ponderal Index, head circumference, chest circumference, gestational age, you know, neural tube defects. And, you know, multiple studies for each of those. And, you know, in one case, for instance, you know, many of these studies also did look at other metals, which I think was kind of

critical, not all of them, but, you know, for instance, there's one study of neural tube defects that actually showed, you know, cases had higher manganese and lead, but then nothing -- you know, there was no association with nickel, and mercury, and arsenic, and so forth. So, you know, that's -- that's a strong literature.

The neurodevelopment literature also cognitive development in preschoolers and infant development. Here, you see U-shaped relationships in many of these studies and some -- some with, you know, fairly large sample sizes. So I think it's a strong literature. And, you know, very -- some robust -- very robust studies I've highlighted. You know, I kind of made my own little spreadsheet. And I've got, you know, several good -- really good strong studies that I think the methods were appropriate and so forth from different countries, and neurodevelopment being definitely one where there's a pretty good literature with good control for confounding.

And then turning to the reproductive -- female reproductive and male reproductive outcomes, again some good studies, and, you know, more on the female side, I think, perhaps, but I think that this is -- this is -- there's -- this -- if it weren't for the essential element part, I would say absolutely this is a high priority. But with it being an essential element, I do have concerns

about how -- how we should be approaching it and really what I would recommend.

CHAIRPERSON LUDERER: Thank you, Dr. Hertz-Picciotto. I think, Dr. Sandy, did you have a comment on that concern that was just raised?

DR. SANDY: I'll see if Carol wanted to say something first.

Carol, I think you're muted.

CHAIRPERSON LUDERER: Still muted.

MEETING MODERATOR: Carol, if you can hear me, so it does show that you're unmuted. If you go to where it has the microphone option on the audio tab, make sure that it didn't switch over to a separate speaker or something like that or you could be muted on the headset itself.

Yeah we're still not hearing you. Is it there by chance a button on your headset that could be muted possibly?

(Laughter.)

CHIEF COUNSEL MONAHAN CUMMINGS: Can get it to work.

CHAIRPERSON LUDERER: Now, it's working.

MEETING MODERATOR: You are. You're there.

CHIEF COUNSEL MONAHAN CUMMINGS: Oh, my gosh. Okay. I'm not going to touch it ever again. Very sorry.

But I just wanted to address the questions about

the essential element issue. And you may or may not know that we have vitamin A listed under Prop 65. And one of the -- the way that the Committee addressed it was to kind of put parameters around it. And say up to this amount is necessary, but above this amount is -- can be toxic. So even though it's on the list, it's not just kind of every exposure to this chemical can cause these effects. And so that's -- that's an option for us in the future. You know, if we get to the point of listing it, we can -- we can certainly talk to you about how you want to approach that.

In terms of the warning, there's no mandatory warning language. The statute just says clear and reasonable warning. We have regulations that provide examples for businesses to use. And recently we updated those regulations and we are periodically adding additional ones for either certain types of exposures or certain chemicals.

And so in the future, if we needed to, we could add one for essential nutrients or for this chemical in particular. So I think we have ways to address that issue under the law. And so -- but for the most part, it would be addressed later in the process. Does that help?

CHAIRPERSON LUDERER: Thank you.

Dr. Allard, you had a comment or question?

COMMITTEE MEMBER ALLARD: Yeah, just a clarification. I was wondering if one of the distinctions can be naturally occurring, so sort of distinct from the level question, naturally occurring versus exogenously added to products. Is that one of the distinctions that can be made in the process?

CHIEF COUNSEL MONAHAN CUMMINGS: Yes. We have a regulation that addresses naturally occurring chemicals, either that are intentionally added or intent -- or, sorry. The source is from human sources or it just is taken up by a plant, for example, and so somebody is exposed through consumption. So we do have a regulation that addresses that -- that issue of naturally occurring.

CHAIRPERSON LUDERER: Okay. Dr. Breton.

COMMITTEE MEMBER BRETON: I just wanted to -- just to further clarify, when you were saying like with vitamin A as an example, does that mean that the label itself could have language on it that indicated an optimal range, let's say, or -- and so that you could specify both going below or going above may be harmful. Is it on the labels themselves that the (inaudible) would see.

CHIEF COUNSEL MONAHAN CUMMINGS: I have not seen a label for that. Labels aren't actually required under Prop 65. You can give warnings in a variety of ways. But based on the listing, you could say, you know, that

exposure to this chemical above X is known to cause reproductive effects.

However, this is a, you know, necessary element and so keep your dose below whatever the other X is, right? So -- so we -- we can't address it that way. And that's why I was saying we could come up with our -- with a specific warning that would address those issues, if the chemical gets listed.

(Multiple voices.)

DIRECTOR ZEISE: Jump in here too real quick. Hi. This is Lauren at OEHHA. The way that vitamin A is listed, it really is listed in a way that precludes a need to warn for levels that aren't harmful. So the way -- the actual listing of it did include a parenthetical. So that would be something to look at as well.

Of course, if we got to that point, if the Committee considered it, we would look to the Committee for their guidance on that.

COMMITTEE MEMBER HERTZ-PICCIOTTO: I think the difference between -- possibly a difference between vitamin A and manganese is that -- I mean, both of them, you know, you can get exposed through the diet, but manganese also has these exposures through air and water and occupational situations which I'm not sure any of those would apply to vitamin A, where in other words a

person can control what they eat, but they can't always control what's -- other sources that they may be getting and they may not be aware of them. So it's well and good to say well we need this much, but then beyond that how will they know what they're actually getting.

CHAIRPERSON LUDERER: Dr. Pessah, you had a question/comment?

COMMITTEE MEMBER PESSAH: Yeah. Where I found it very difficult was there seems to be overlapping ranges in exposures, doses for both the biological -- the important effects of manganese and those that might be obtained through -- sort of nutraceuticals that may be charged up in manganese. And those dose ranges would overlap and maybe even, of course, be added to it depending on the time of day that the intake occurred.

So I don't think it -- you can clearly break the physiological levels from those that would be considered adverse. I think they overlap and can be additive.

CHAIRPERSON LUDERER: Any other comments or questions on manganese?

PUBLIC COMMENT

CHAIRPERSON LUDERER: Do we have any public comments, Jessica, requests for comments?

MEETING MODERATOR: I do see a hand raised from Donna. It has been up a while, so I'm not sure if it's

regarding this. So I am, Donna, going to lower your hand. And if you do want to mute -- actually you unmuted yourself. I'll go ahead and let you speak.

DR. FARMER: No, it was not about this. It was earlier on glyphosate.

MEETING MODERATOR: All right. So then -- yeah, so no hands raised regarding what we just -- what we just spoke to.

CHAIRPERSON LUDERER: All right. Okay. Thank you. Any further discussion by the Committee?

COMMITTEE DISCUSSION AND RECOMMENDATION

CHAIRPERSON LUDERER: Okay. We can then move on to our final recommendation. So we have high, moderate, and no concern.

So please raised your hand if you believe that manganese should be considered a -- of high concern.

(No hands raised.)

CHAIRPERSON LUDERER: All right. I see no hands.

Moderate concern?

(Hands raised.)

CHAIRPERSON LUDERER: I see, Dr. Plopper, Dr. Woodruff, Dr. Baskin, Dr. Carmichael, Dr. Breton, Dr. Auyueng-Kim, Dr. Hertz-Picciotto, Dr. Pessah, Dr. Allard and Dr. Luderer.

Okay. So everyone is in the moderate category.

Thank you.

NEONICOTINOID PESTICIDES

COMMITTEE DISCUSSION

CHAIRPERSON LUDERER: So then we will move on to our next -- this is a group of chemicals, the neonicotinoid pesticides, acetamiprid, clothianidin, imidacloprid and thiamethoxam. And since we have to vote on each of these separately, I think the -- and we have several -- we have parabens coming up too and PFASs where we have to do that, I'm going to propose that we discuss them one at a time and then vote after each one after we've discussed it, unless there's -- there are objections to that. I think that might be the simplest way to do this.

Tracey -- or Dr. Woodruff.

COMMITTEE MEMBER WOODRUFF: Just -- yeah, I'm just thinking I want -- I guess we can't consider them as a group. I don't know. It's kind of --

CHAIRPERSON LUDERER: I mean, the database is not going to be different.

COMMITTEE MEMBER WOODRUFF: (inaudible.) So it's -- anyway. Okay. That's fine. I guess I would prefer to discuss it as a group and then go through them individually, I mean, because they have just like a similar mechanism of action. You know, studies -- while

studies have been done individually, they are relevant across the chemical. That's why it's a little bit complicated.

CHAIRPERSON LUDERER: How -- okay. So the discussants are Dr. Woodruff, Dr. Carmichael, and Dr. Plopper. How do the other discussants feel about that?

COMMITTEE MEMBER PLOPPER: That was one of my concerns too. And not only do these look the mechanisms are the same and some are not as thoroughly studied as others, but the result is about the same.

COMMITTEE MEMBER WOODRUFF: Right.

COMMITTEE MEMBER PLOPPER: And the other is that one of them is a metabolite of another one.

COMMITTEE MEMBER WOODRUFF: Right. Right.

COMMITTEE MEMBER PLOPPER: So those two should be definitely considered together. So, you know, my concern is the one that produces a metabolite, how do we know when we're looking at what's the effect of identified as treatment with that chemical is not actually the result of the metabolite. That was -- that's my concern. I think if there were some way we could do it that way, I think it would be very useful, because we're not -- well, anyway.

CHAIRPERSON LUDERER: So discussing them all as a group, is that your preference?

COMMITTEE MEMBER PLOPPER: That would be my

preference too, because I think like she said, it would be more effective in -- and like I said, one of them is a metabolite of the other, so we can't really discuss them separately anyway --

CHAIRPERSON LUDERER: Okay.

COMMITTEE MEMBER PLOPPER: -- because we don't know if it's that one or the metabolites that's the problem.

CHAIRPERSON LUDERER: Dr. Carmichael.

COMMITTEE MEMBER CARMICHAEL: It's fine with me. Yeah, it's fine with me too and the epi is going to be very brief.

CHAIRPERSON LUDERER: All right. Okay.

DOMOIC ACID

COMMITTEE DISCUSSION AND RECOMMENDATION

COMMITTEE MEMBER ALLARD: I (inaudible) the conversation, but I just -- I'm just noticing in the chat that Dr. Cogliano has been waiting to make an intervention about the domoic acid since before the lunch break.

CHAIRPERSON LUDERER: Oh. Oh, no.

COMMITTEE MEMBER ALLARD: And so we just -- I just want to make sure that at some point we go back to it.

CHAIRPERSON LUDERER: All right. Well, we -- why don't we -- well we can do that now, since we haven't

started the discussion yet, if Dr. Cogliano would like to give us that information.

DR. COGLIANO: Yes, I'm able to do that. Thank you very much. So the question was about the levels of Cal -- that California uses in relation to other Pacific states. And California uses the FDA actual levels, where we would take action if the level in crab meat or any other seafood exceeded was greater than or equal to 20 parts per million. Oregon and Washington do the same.

Now, there's a separate one for viscera of dungeness and rock crab, where FDA and California say to take action above 30 parts per million, because people eat less of that. Oregon and Washington banned it at equal to or 30 parts per million. So it's a very, very, very minor difference.

The other thing that we uncovered -- our staff is really great. I mean, they -- thy jumped right on this. So there are more recent studies that show neurotoxic effects in humans and in non-human primates as lower levels than these action levels. And this would also suggest a concern for developmental neurotox. But these are neurotoxic on studies. Neurotox studies not developmental neurotox studies by and large. The developmental neurotox studies that we were able to find are summarized in your large document.

CHAIRPERSON LUDERER: Okay. Thank you very much for getting us that information. Since we just heard that and we have not voted yet on domoic acid, perhaps we should go back and complete that vote before continuing with the neonicotinoid pesticides. And thank you, Dr. Allard, for noticing that in the chat.

All right. So then we will vote on domoic acid. So please raise your hand if you believe that we should rank domoic acid as being a high priority.

(No hands raised.)

CHAIRPERSON LUDERER: Okay. I'm not seeing any hands.

Moderate -- is that for high, Dr. Pessah, or moderate?

Were you voting for high or moderate?

COMMITTEE MEMBER PESSAH: That was high.

CHAIRPERSON LUDERER: Okay. All right. All right. So one for high. I think I didn't miss anyone else. All right, Dr. Pessah, for high.

And then do we have any people voting for moderate priority.

(Hands raised.)

CHAIRPERSON LUDERER: Okay. Dr. Plopper, Dr. Woodruff, Dr. Carmichael, Dr. Breton, Dr. Auyeung-Kim, Dr. Hertz-Picciotto, Dr. Allard, and Dr. Luderer.

And anyone considering -- I think I said Dr. Baskin. No, if not. All right. All right. Dr -- then we have one -- is there a vote for no priority?

(No hands raised.)

CHAIRPERSON LUDERER: Okay. All right. That's what -- so then we are -- we have finished then with domoic acid.

NEONICOTINOID PESTICIDES

COMMITTEE DISCUSSION

CHAIRPERSON LUDERER: And we'll go back to the neonicotinoid pesticides. So as we just, I think, concluded, we would discuss these -- or the discussants thought it would be better to discuss them as a group.

So, Dr. Carmichael, would you like to start with that?

COMMITTEE MEMBER CARMICHAEL: Sure. I'll just summarize that epi studies briefly and then I assume the others can get into more detail the -- more broadly the mechanisms and so forth.

So two of these had no epi studies, so those are quick, the clothianidin and the thiamethoxam. And the acetamiprid had one human study -- human epidemiologic study that is. And it was suggestive, but very small, and once again it was just one study. It was 65 pre-term low birth weight babies who were admitted to the NICU in one

hospital in Japan. They looked at urine samples at birth and at two weeks and they only really had much detection of a metabolite. They measured seven different neonicotinoids, but only really detected this one metabolite of acetamiprid. And it was detected in a quarter of the newborn samples and only 12 percent of the samples they took two weeks later. They did test suggested findings of a higher detection rate and the babies who were small for gestational age.

But it was a really -- it was an odd analysis in that they were -- they were putting together the samples that they took from the same babies at two different time points. So that's all there is there.

And then for imidacloprid -- I'm sorry if I'm mispronouncing any of these. There's basically two studies. One is three publications, but they're all from the national birth defects prevention study and I'm a coauthor on those. That is a large population-based case control study. And it was based on California participants in that study and whether they lived within five a 500 meter radius of resident -- of proximity to commercial agricultural pesticide applications. And this was based on the Pesticide Use Reports in California. Looked at a bunch of different compounds from 10 to 30 different chemicals per birth defect that actually had

enough exposures to be able to study them, which was set at at least five exposed cases. So we looked -- we actually looked at a ton more chemicals, but didn't have the power to look at them, because they were less frequent.

Basically, in summary, looked at a number of different structural anomalies and found modest suggestive associations with this compound and gastroschisis, one congenital heart defect, and anencephaly and orofacial clefts. But again, these -- they were in the range of, you know, 1.5 to around two-fold increased risk or odds ratios. And it is the only study that we're aware of that -- who had -- we called it hypothesis generating, because other studies had looked at these compounds specifically for these outcomes, so that's what there was in that sort of area.

And then the other study that was listed in our materials was a study of autism by Keil and others, including Dr. Hertz-Picciotto. And they did find modest association of use of products that in -- for flea and tick control on pets that include this ingredient and found that consistent users had a two-fold increased risk. Again, it was suggestive, but it is a -- it's the only study about -- that I'm aware of, at least that was in our -- I didn't do a full literature search beyond what

was in our materials. But that is the summary of the epidemiologic literature we have before us.

CHAIRPERSON LUDERER: All right. And did -- let's see, our next discussant is Dr. Plopper.

COMMITTEE MEMBER PLOPPER: Okay. Well, there -- the animal toxicology studies kind of vary in number and the subjects that they focused on. And the one that had the most was the imidacloprid. And it's a metabolite of the -- of one of the others. And the areas that seem to be the -- have the most problem or show the most changes from animal to animal were in the impact on development and growth of offspring and negative impacts on the brain, in terms of failure to do these various tests.

And for some of the chemicals, there was -- some didn't -- most of them didn't look at it, but those that did found changes in various endocrines related to testosterone and various androgen receptors. The female reproductive studies, so changes in the ovary and in -- again, in estradiol and LH and FSH levels, and progesterone levels.

And in males, it seemed to be consistent that there was some sort of a pathology in the testis, as well as the inability of the sperm to function either through motility or viability. And there were large numbers of mutations. And the number of sperm production was

dropped. And it's variable. I don't know if you want to go through chemical by chemical, but it's variable, the amount of study in each one of them.

But they also -- when they had the same -- looked at the same subject, it tended to be pretty much the same result. The one that did the most on the brain found that the hippocampal area was really damaged. So I'll just stop there. I don't know if -- let Tracey do the rest of it.

CHAIRPERSON LUDERER: Okay. Yeah, I think at the -- once all three of you have spoken, I think maybe we'll ask you for your preliminary kind of thoughts on the priority.

So, Dr. Woodruff.

COMMITTEE MEMBER WOODRUFF: Yes. Thank you for the previous comments. I just want to note that this mechanism the neonics act on cen -- or a cen -- act on the central nervous system, in terms of they act on the nicotinic acetylcholine receptors and prevent acetylcholine from transmitting. So sort of similar to the organophosphates. And it's true the most studies were on imidacloprid. And there aren't very many human studies, but there are quite a few animal studies.

And I think the thing that I was expecting was to see more neurodevelopmental studies, but there are quite a

few studies looking at exposures and effects on male reproductive health. So the findings indicate effects on male reproductive organs including seminal vesicles, epididymis, testes, and effects on sperm, including reduced sperm concentration, reduced sperm mobility and viability, increased sperm abnormalities. And this was also studies on changes in male reproductive hormones, including a number of studies, I think Dr. Plopper mentioned this, that reported decrements in testosterone measurements. So that's some consistency across those findings.

And while there were some studies -- I mean, you know, across any science, there's some studies that there's variability in findings. But I would note that the studies that looked at more chronic exposures were more likely to find studies in the ones that didn't find effects. And the ones that didn't, tended to be more short-term, acute exposures.

So I thought that was -- actually, the male reproductive effects studies were quite compelling. There were a number of studies looking at neurodevelopmental effects, some of the more guideline studies and saw various responses, including decrease in auditory startle response, decreased performance in certain types of tests. And that -- albeit, there's only one study in humans that

is somewhat consistent with that.

And then there were some studies looking at effects on birth defects. So skeletal variation, so decrements in pup weights, but essentially developmental effects that were again, you know, these -- kind of like we're looking at the prioritization, but it wasn't inconsistent or could be consistent with the very small number of human findings.

Finally, there were also female reproductive effects, including effects on the ovaries, the ovarian damage, decreased ovarian weights, effects on ovarian follicle development. And similarly, as Dr. Plopper mentioned, there were also observations of effects on hormones related to that.

And I just -- I noticed when I was looking at this, that the State of Michigan has done a review of this, because they reviewed the toxicity -- I'm sorry, not Michigan, Minnesota -- for their water quality guidelines. And they noted that they also found similar effects. So they found developmental effects, reproductive and neurotoxicity effects for imidacloprid, clothianidin, and thiamethoxam.

So I -- just looking at the -- well, so anyway. That's my story. Now, I know you want to talk about them individually. I'll have to think about that for a minute,

so...

CHAIRPERSON LUDERER: Okay. Do we have -- maybe we'll start again with Dr. Carmichael, did you have preliminary thought about what the priority?

COMMITTEE MEMBER WOODRUFF: Yeah, I would just say -- so, I wanted -- I wanted to start, because I just think the male reproductive effects were pretty compelling across these studies, so I --

CHAIRPERSON LUDERER: Okay.

COMMITTEE MEMBER WOODRUFF: -- I just think that from that perspective, I would rank this as high, given that this is a pretty widely used pesticide. Though I have to -- you know, I -- I look at it as a group, so I want to think about how I would rank them individually.

CHAIRPERSON LUDERER: So high for the group is what your -- your first thought.

COMMITTEE MEMBER WOODRUFF: Um-hmm.

CHAIRPERSON LUDERER: Yes.

Okay. Dr. Carmichael.

COMMITTEE MEMBER CARMICHAEL: Just one other point to make, I'm not sure if any of us made it, is that the -- the poundage that's applied to your is like at least 10-fold higher for imidacloprid than the other ones -- than the other three, so I --

COMMITTEE MEMBER WOODRUFF: Right.

COMMITTEE MEMBER CARMICHAEL: And it -- and I'm just not sure if there was more evidence. I think maybe one of you said there was more evidence on that one than the other ones tended to be and --

COMMITTEE MEMBER WOODRUFF: Right.

COMMITTEE MEMBER CARMICHAEL: -- it may for that reason.

COMMITTEE MEMBER WOODRUFF: Yeah. So maybe that's the way to prioritize it, because it's used at a higher rate, but you --

COMMITTEE MEMBER CARMICHAEL: Depending on how approach it, yeah, that would be the one that sounds like it's higher -- higher -- more commonly an exposure.

CHAIRPERSON LUDERER: Dr. Plopper.

COMMITTEE MEMBER CARMICHAEL: So in that vein, I mean, for that one I would tend towards a higher more moderate. Not a no for me.

CHAIRPERSON LUDERER: All right. Dr. Plopper.

COMMITTEE MEMBER PLOPPER: I would agree. I thought the male reproductive information was very -- very compelling. And I -- I would have no problem ranking them based on how much is actually used here. But I think we should also consider the ones -- one that's a metabolite and make sure that the -- that the parent compound is considered at the same time.

COMMITTEE MEMBER WOODRUFF: Yeah, that's a good recommendation. I agree with that.

COMMITTEE MEMBER CARMICHAEL: So which ones are metabolites of each other? I had just written down that --

COMMITTEE MEMBER WOODRUFF: Well, yeah, I have that this one is just a DMAP is a metabolite of acetamiprid. (inaudible)

COMMITTEE MEMBER PLOPPER: I'll have to --

COMMITTEE MEMBER CARMICHAEL: Clothid -- clothianidin is a metabolite of thiamethoxam. I'm sure took -- I'm not sure where I took that from.

COMMITTEE MEMBER PLOPPER: Yes.

COMMITTEE MEMBER WOODRUFF: Yeah, yeah. That's what you -- right.

COMMITTEE MEMBER CARMICHAEL: And then DMAP is a metabolite of the -- which one.

COMMITTEE MEMBER WOODRUFF: It's -- that's the metabolite acetamiprid.

COMMITTEE MEMBER PLOPPER: Yes.

COMMITTEE MEMBER CARMICHAEL: Okay. And that was in that one study that I viewed. Yeah, okay. But that wasn't -- that's not something that we studied as --

CHAIRPERSON LUDERER: Separately, right. Yeah.

COMMITTEE MEMBER WOODRUFF: Oh, well. Now,

that's not covered. You're right.

(Laughter.)

CHAIRPERSON LUDERER: All right. Any comments from any of the other panel members?

Dr. Allard.

COMMITTEE MEMBER ALLARD: Yeah, I'm probably going to open a can of worms here, but, you know, that what's interesting about neonicotinoids is that they were designed to affect the cholinergic system, but with a specificity for non-human species. But I was kind of going back to our mandate. And the fact that we are looking at these chemicals from the ability to cause reproductive toxicity and it actually does not specifically say humans. And when we think about beneficial species like these and the weight of evidence showing that these chemicals kind affect -- can actually be at the root of colony collapse disorders, I was wondering whether we should put that -- the reproduction of other species, beneficial species into -- into the balance and not just focus perhaps too narrowingly on ourselves or rats and mice.

CHAIRPERSON LUDERER: Thank you for that comment. And perhaps the staff have a -- can say something about that. But first, I know Dr. Pessah had his hand raised.

COMMITTEE MEMBER PESSAH: Well, I teach this

stuff to veterinarians every year. And the data on beneficial insects is quite damning, I think. The reproductive effects, you know, this experiment has been done on millions, and millions, and millions of domesticated animals constantly and many of them are high valued breed specific. You think that one would have picked up on reproductive effects just from adverse reporting. And I don't really see this in the literature. Now, not scientific, but breeders are, you know, very sensitive to anything that affects the reproductive success of their animals.

And with respect to production, that hasn't shown up in any of the sort places you would think you'd pick it up. But in terms of what Dr. Allard just said, that is a huge issue. And if we need to consider that, that would move up the priority for me, but otherwise, I think it's probably in the moderate.

CHAIRPERSON LUDERER: Do we have any input on that question from staff?

CHIEF COUNSEL MONAHAN CUMMINGS: Yeah. This is Carol. I think that the way that Prop 65 has always been interpreted is that it's warnings for human exposures to chemicals. We can rely on animal studies to identify those chemicals, but it isn't designed to address kind of environmental issues like bees directly. So I don't -- I

don't think you can really take that into account on -- in terms of plop 65 not to say it isn't important, but it's -- it wouldn't raise the priority or make us, you know, list a chemical based on the effects on bees directly, if that helps.

CHAIRPERSON LUDERER: Yeah. Thank you for that clarification.

PUBLIC COMMENTS

CHAIRPERSON LUDERER: I know we have a number of public comments, so why don't we turn to the public comments and then we can have further discussion after the public comments from the group.

So, let's see. I see that we have -- these are organized by the agent somewhat. So for acetamiprid Keith Morris-Schaffer from Exponent requested comment. Jessica, is -- can you unmute him?

MEETING MODERATOR: Absolutely.

CHAIRPERSON LUDERER: Yes.

MEETING MODERATOR: And I see Keith. So Keith, I'm going to go ahead and unmute you. Just go ahead and press the button on your side as well and then we can hear you.

DR. MORRIS-SCHAFFER: Can you hear me?

CHAIRPERSON LUDERER: Yes.

MEETING MODERATOR: Yep.

DR. MORRIS-SCHAFFER: Okay. Thank you.

Good afternoon, everyone. My name is Keith Morris-Schaffer and I'm a toxicologist with Exponent in our Sacramento office, speaking on behalf of Nippon Soda and their United States branch, Nisso America, which is the primary distributor of acetamiprid-based pesticide formulations in the U.S.

We appreciate the opportunity to speak to you all today and we appreciate the Committee members, particularly the lead discussants, who reviewed acetamiprid. And I've spent time reviewing the literature and providing thoughtful comments of their own.

As we presented in our written comments, we do respectfully request that DARTIC consider each of the neonicotinoids on an individual basis for the purposes of prioritization. The four neonicotinoids listed for prioritization by OEHHA are four disparate compounds with unique physical, chemical and toxicological properties that should be evaluated independently.

The United States Environmental Protection Agency has very recently stated that the neonicotinoids present a broad spectrum of different insecticidal properties and outcomes and that based on its generalized toxicological profile from animal studies, acetamiprid does not, in fact, have a recognized common mode of action with other

substances.

Furthermore, as presented in our written comments, there's no indication that in the published or unpublished literature that acetamiprid has a mode of action that's specific to male reproductive or developmental toxicity.

And just with regards to more detail on mechanism, it should be noted that, as Dr. Allard I think said, they were designed originally to target insecticidal nicotinic acetylcholine receptor subtypes. However, at the same time, they're also shown to have magnitudes less binding and interaction potential for mammalian nicotinic acetylcholine receptor subtypes in the central nervous system.

As such, there's very limited evidence that neonicotinoids can have direct adverse impacts on the central nervous system of mammals. Their toxicity profiles, including histopathology, clinical pathology, and behavioral observations of mammals are much more indicative of generalized toxicity mode of actions, rather than preferential targeting of nicotinic systems. And this was supported in a good review in 2016 Sheets et al., which was in the OEHHA documents, which found substantial differences between nicotinic based NT outcomes and the variety of outcomes presented in neonicotinoid

developmental neurotoxicity studies.

It's also worth noting, because I know this was brought up, that acetamiprid does not have a parent or metabolite relationship with the other three neonics at hand for discussion. The DMAP metabolite that was brought up, that was just a metabolite used as a biomarker exposure in a epi study, and the one epi study for acetamiprid. And these chemicals really shouldn't be evaluated as a group, as their toxicology endpoints and results are specific to each chemical.

I think Dr. Carmichael did a great job reviewing the acetamip -- the one acetamiprid epi study and she got her points across regarding that's very limited -- and as such, since there's only one study, it doesn't really pass OEHHA's screening prioritization criteria, which requires two studies.

So based on sort of the lack of human data for acetamiprid, there's a significantly higher burden to have very strong evidence from animal studies to support that acetamiprid poses a significant hazard. However, based on the -- a comprehensive review of these animal toxicity studies, there's no indication that acetamiprid is a male reproductive or developmental toxicant.

There's an extensive database of high quality guideline studies for acetamiprid that have directly

evaluated male reproductive and developmental outcomes. It's also worth noting that all -- that some of these guideline studies, particularly the ones that are investigating chronic and subchronic exposure across multiple species, mice, dogs and rats, were not, in fact, in the OEHHA document, so there might have been limited exposure to those guideline studies looking at male reproductive outcomes.

However, these studies and all their data are rigorously reviewed by regulatory agencies, including consideration of statistical and biological significance as part of the pesticide registration process. And as we presented in our written comments, all six guideline studies that directly evaluated the effects of acetamiprid on male reproductive outcomes and thus the two guideline studies on prenatal-only exposure developmental outcomes, none of these studies indicated any adverse outcome.

And this interpretation is very consistent with U.S. EPA, with the California Department of Pesticide Regulation, with the World Health Organization, and in a very, very recent review in 2018, the European Chemicals Agency Biocidal Products Committee.

With regards to the published literature on acetamiprid male reproductive outcomes, the studies have quite a few limitations. Some of them are using pesticide

formulations and not directly evaluating acetamiprid itself, and some of them can also just be attributable as a second consequence of general system toxicity with no male reproductive specific hazard.

With regards to developmental outcomes, there's really only very few studies looking at DNT outcomes. And most of them essentially have a postnatal exposure window. And the endpoints of interest are occurring after that postnatal window. And the basis of a developmental listing under Proposition 65 is specific to effect on the conceptus or in utero exposure. And it's difficult to --

DIRECTOR ZEISE: Excuse me, if I could just interrupt. We don't have a bell or a light to show, but the five minutes are up, Ulrike. I just wanted to let you know.

CHAIRPERSON LUDERER: Okay. Thank you.

DR. MORRIS-SCHAFFER: Okay. So just -- I guess I'll -- just to note that again since the basis for developmental listing under Proposition 65 is in utero exposure alone or affects on the conceptus, by having studies that include a postnatal window and looking at endpoints after that, it's again difficult to attribute that effect to an in utero exposure.

And I guess to conclude, we could just say we respectfully request the four neonicotinoids be considered

separately when considering and voting on prioritization, and we also request the DARTIC Committee recognize that acetamiprid on its own does not currently pass OEHHA's screening criteria for prioritization. Therefore, acetamiprid should be identified as no or low priority for hazard evaluation.

Thank you.

CHAIRPERSON LUDERER: Thank you. Thank you, Dr. Morris-Schaffer. Let's see, I have listed that there's another person, Dr. Jay Murray, who would like to speak to acetamiprid as well. Do you have Dr. Murray?

MEETING MODERATOR: Yes. All right.

CHAIRPERSON LUDERER: Okay.

MEETING MODERATOR: Dr. Murray, I'm going to go ahead and unmute you. You should be able to speak now.

DR. MURRAY: Okay. Can you hear me?

MEETING MODERATOR: Yes, we can.

CHAIRPERSON LUDERER: Yes.

DR. MURRAY: Good. Well, thank you. This is Dr. Jay Murray. And most of you know me. For those who don't, I'm a toxicologist, a former member and Chairperson of this Committee. And I'm speaking on behalf of the companies responsible for the other neonic pesticides on your agenda, that's the second, third, and fourth on your agenda.

I've got two points. The first is I encourage you to prioritize all four neonics individually, not as a class. This morning, Dr. Pessah mentioned organophosphates as an example of a group of chemicals that should not be treated as a class and neonics is a similar example. The late Dr. John Casida at UC Berkeley was one of the world's leading experts on the toxicity of neonics. And his reviews show each neonic has a different profile of effects on the various nicotinic acetylcholine receptors that occur in mammals.

And Dr. Allard correctly noted that the neonics are designed to take advantage of differences in the binding affinity of the neonic or nicotinic receptor that exist in insects compared to nine or more nicotinic receptors that occur in vertebrate species.

So depending on the specific neonic, the effect on the receptor is not the same. It can range from weak stimulation, to potent stimulation, to blocking the receptor for stimulation. So you wouldn't affect -- you wouldn't expect them to all have similar activities.

Some neonics produce evidence of transient nicotinic signs at high doses, but others do not. And for those reasons, the neonics should be prioritized individually not as a class.

Second, I urge you to consider the importance of

maternal toxicity in prioritizing the developmental toxicity of neonics. Prioritization procedure as well as your listing criteria address the maternal tox issue. And historically, this Committee has considered the relationship between maternal toxicity and developmental toxicity. And chemicals that cause developmental toxicity that is not secondary to maternal toxicity have been the ones more likely to be assigned a high priority.

Prop 65 is not focused on all aspects of toxicity. It does not address systemic toxicity, instead focusing on cancer and reproductive toxicity only. So as stewards of Prop 65 resources, I encourage you to emphasize chemicals that show effects in the absence of maternal toxicity over those that do not.

Thank you. And I'd by happy to respond to any questions.

CHAIRPERSON LUDERER: All right. Thank you very much, Dr. Murray.

DR. MURRAY: Thank you.

CHAIRPERSON LUDERER: We have -- yeah, and we have several additional speakers who wish to speak I believe about clothianidin. Edward Scollon, I hope I'm pronouncing that correct, from Valent USA. Jessica, do you have Dr. Scollon, can you unmute him?

MEETING MODERATOR: I sure do. Okay. So I'm

going to go ahead and unmute you know. And you should be able to unmute yourself and speak.

DR. SCOLLON: Thank you. I appreciate that.

So I want to start by saying good afternoon. And to the Committee, I appreciate the time you have taken to review clothianidin and all the other nico -- neonics on the list.

So for today I'm going to just focus on the developmental -- well, actually, let me back up one -- one thing here. So there was some discussion about degradates for these neonics. And so clothianidin is the degradate of thiamethoxam. So even though clothianidin is a degradate, there are separate risk assessments for each of these chemicals. And they do have varying affects as some of the previous speakers have already noted.

So I'm going to focus again just on clothianidin and I'm going to really just spend a few minutes talking about the developmental neurotox -- developmental neurotoxicity effects that were identified in the DARTIC prioritization document. Following me, my colleague from BASF, Dr. Brandy Riffle will speak on reproductive developmental considerations for clothianidin.

So this has already been brought up, but clothianidin has been registered for use by the U.S. EPA and Canada's PMRA, as well as several other regions

throughout the world, including Australia, Asian Pacific, and the European Union, since the early 2000s. So it's been registered for a while.

And each of these regulatory agencies have determined that the label uses of clothianidin do not pose a risk to human health. So more specifically, the recent EPA risk assessment in 2017, as well as the PMRA assessment in 2011, have determined that the risks for reproductive and developmental effects are low for all registered uses, as well as the JMPR, which is the FAO WHO joint meeting on pesticide residues.

In 2010, they determined that clothianidin induced developmental toxicity only in the presence of maternal toxicity. And it was -- it is not teratogenic in that clothianidin is not a developmental neurotoxicant.

It -- speaking to some of the effects that were observed in the guideline studies, so the -- regarding the developmental neurotoxicity study, which has been mentioned previously, findings in this study included increased pup mortality in the high dose group, as well as the decreased auditory startle response again in the mid- and the high-dose groups.

So one of the things I want to point out is that both the decreased pup body weight was also observed in the mid-dose and the high-dose groups. So it's difficult

to attribute the affects to developmental neurotoxicity when including their systemic toxicity.

And then furthermore, and probably more importantly, there is no supporting histopathology or other indications of neurotoxicity in the database of toxicological studies. And again, as this has been previously pointed out, that there are numerous studies in the database, including studies in rats and rabbits, and chronic studies in the rat, mouse, and dog.

Also, there were a couple of studies -- literature studies that were mentioned in the prioritization document and that appeared to support developmental neurotoxic findings. However, these papers, Ozdemir 2014 and the Tanaka 2012, so although singular findings were observed for each these studies, the weight of evidence -- the weight of the results are decreased by limitations within these literature studies.

So finally, I just want to conclude that by in contrast -- in contrast, the reviews by the regulatory agencies relied on guideline studies, which use a higher number of animals, appropriate statistical methods, and they have historical control data which is used to refine the interpretation of the study results.

And therefore, based on the weight of evidence provided by the existing studies, it's clear the

clothianidin is unlikely to propose a human health concern regarding developmental toxicity.

So with that, thank you for your time again, and if you have any questions, I'll be happy to answer them now.

CHAIRPERSON LUDERER: Okay. Thank you very much.

I think we will move on to the next commenter, which I believe is going to be Brandy Riffle from BASF.

Jessica, can you unmute, Dr. Riffle.

MEETING MODERATOR: Yes, finding the name here. Let's see.

CHAIRPERSON LUDERER: R-i-f-f-l-e.

MEETING MODERATOR: Here we go. All right, Brandy, I'm going to go ahead and unmute you. You should be able to unmute yourself here in a few seconds. There we go.

DR. RIFFLE: So thank, Jessica. Can everyone hear me okay?

CHAIRPERSON LUDERER: Yes.

DR. RIFFLE: Wonderful. Well, hello. Good afternoon. Again, my name is Dr. Brandy Riffle. I'm a regulatory toxicologist with BASF. And I have responsibility for clothianidin, as well as expertise and training in endocrine toxicology. And again, thank you so much for allowing me a few minutes to provide some

additional information for consideration today in your prioritization of clothianidin.

I would like to focus my comments to specifically those regarding the male reproductive toxicity of clothianidin. First, we do have both a multi-generation reproductive study in the rodent that was conducted with clothianidin, the guideline study, and it is used to support the registrations globally.

In that study, there were no adverse findings on male fertility. There were some slight effects in sperm motility that were noted. However, these were in animals that had a body weight decrement of 19 percent.

So in 1997, a publication from Chapin et al. noted in rodents that body weight reductions of 10 percent or greater compared to control animals can likely impact sperm motility in rodents. And thus, we think the findings that we see -- the very slight findings we see in the male reproductive study are due to general systemic toxicity and are not relevant for a reproductive hazard classification.

Moving on to the literature that has been provided and cited by the DARTIC Committee, I'd like to discuss several of the studies.

In general though, there were some findings in the studies. The overall conclusions from Yanai et al. in

this 2017, Bal et al. in 2013, as well as some of the others, were that there were no relevant findings on either androgen-related parameters following treatment with clothianidin or that clothianidin had little detectable detrimental effects on the reproductive system of male rats over the measured parameters.

Additionally, clothianidin has been screened using the U.S. EPA's ToxCast in vitro system, and it has -- was without effect for any of the cellular systems that are designed to look for possible effects on the androgen pathway. Again, thank you so much for your time and I'm happy to be here for any questions that you may have.

Thank you.

CHAIRPERSON LUDERER: Thank you very much.

We have another request from Larry Sheets from Bayer Crop Science. I believe it's to speak on imidacloprid. Is Dr. Sheets available? Jessica, can you unmute him?

MEETING MODERATOR: Absolutely.

CHAIRPERSON LUDERER: Thank you.

MEETING MODERATOR: So, Larry, I'm going to go ahead and unmute you. You should be able to unmute yourself now.

Oh, you're self-muted. Go ahead and press it one

more time. There we go.

DR. SHEETS: Okay. How is that?

CHAIRPERSON LUDERER: Good.

MEETING MODERATOR: Perfect.

DR. SHEETS: Is that better? Okay. Thank you. You can hear me then, right?

CHAIRPERSON LUDERER: Yes.

DR. SHEETS: Great. Well, thanks and good afternoon. By way of introduction, I'm a toxicologist with Bayer. I worked with them for 30 years and I specialize in developmental neurotoxicology. I was the study director for the guideline DNT study that's cited in the OEHHA document and also the lead author of that Sheets et al. review paper on neonicotinoids and have an assessment of evidence for developmental neurotoxicity.

And I think that would be a good paper for any of the Committee members who's interested in what is of -- information is available on developmental neurotox or adverse neurodevelopmental outcomes and the association between imidacloprid and other neonics with nicotine and each of the other respective neonics.

My comments today will focus on why imidacloprid should not be prioritized for further review as a developmental and reproductive toxicant. As noted by others, the principal mode of action for some of the

neonics, and in particular imidacloprid the primary mode of action, and what we see at relative lower doses compared to any other findings, is -- is -- are transient nicotinic signs, transient evidence of nicotinic activity.

So in spite of the fact that it's designed to not affect the vertebrate nicotinic receptors, we do see findings -- nicotinic effects at relatively high dose levels, but we don't see developmental and reproductive toxicity. And that's not -- that's not just my determination, that's a conclusion of various authoritative bodies around the world.

So -- so to get into kind of the nuts and bolts of what I want to cover in the next couple -- or three minutes is the point that U.S. EPA, California Department of Pesticide Regulations and the Health Canada PMRA have reviewed the collective body of evidence for imidacloprid several times over the past 30 years that has been registered have no associated concerns for developmental and reproductive toxicity.

That's not that there's absolutely no findings at the high dose. Though what they see is at the -- at high dose levels, the findings are explained based on overtoxicity, maternal toxicity, and such things as that, because as we understand, if the moms are substantially impacted in terms of their health, there are going to be

consequences in terms of the health of the offspring. And that's particularly relevant for rodent species where the mother's health and being able to reproduce again takes priority over the health -- the health and survival of the litter, but I'm getting a little ahead of myself now.

But in terms of the process, the fact that we have these recent reviews from various authoritative bodies, my understanding the process at OEHHA is that a substance such as this should be assigned a low priority for consideration by the Committee, because it has already undergone multiple and recent reviews that includes the information, including the formation that is cited as positive -- for positive findings.

I think one of the things as I look through the information for imidacloprid that I see is missing is all of the negative results. Go through these studies and I say, well, this study shows this finding. Well, what about the negative findings in that study. Oh, there's a negative finding in the -- or, there's a positive findings that are really emphasized. And I think the -- these authoritative bodies look at that information as well, so they have a much broader perspective of the total toxicology picture for imidacloprid than the Committee has available to them.

Under the -- the category of maternal and

developmental toxicity, I would agree with what I understood from the Committee's comment is there's really very little information pointing to maternal and developmental toxicity. There are few findings, but not consistent across studies reported in the literature. And for the guideline studies that are cited, those affects that are seen, like evidence of fetal toxicity, is associated with pretty substantial maternal toxicity, including death of some of the mothers in the rabbit developmental tox study. So that's -- that really puts that into perspective importantly.

Under the comment about neurodevelopmental effects, there was a point made that there are effects reported on learning and memory. In fact, I saw only one developmental tox study that was cited in the OEHHA document for that. There were a couple three studies that cited evidence of pathology or effects on GFAP in the hippocampus.

I can say that I don't see a consistent pattern of that. There's very limited evidence of that. And in our guideline study, we showed no evidence of effects on learning and memory effects on the hippocampus. And if you're interested, I'd be happy to explain the rigor of the guideline study relative to the studies that are cited to support that.

But I think the most important body of evidence that I saw and was noted by the Committee were those evidence of effects on male reproduction and effects on the ovary.

And certainly, there were a few studies there, and -- but I think the thing that's missing again is there's several publications that show no associated effects. And the results of the guideline studies that we run, the developmental tox studies, the two-gen repro studies, the developmental neurotox study showed no such --

DIRECTOR ZEISE: Excuse me for -- excuse me for interrupting, but I'm the five minute buzzer and so your time --

DR. SHEETS: Can I have -- can I have 20 seconds?

DIRECTOR ZEISE: And I'll leave to the Chair. Thank you.

CHAIRPERSON LUDERER: Just please complete your thought and then we need to move on to the other commenters.

DR. SHEETS: Thank you. I appreciate that. The thing I wanted to say is there are multiple studies, almost every study we run, looks at effects on ovary, testis, and evidence of sperm effects. And we have the full complement of EDSP studies that look for effects of

estrogenic and androgenic activity. Those studies were all negative. So I'd -- I would appreciate the Committee considering that in the context of the weight of evidence.

Appreciate your time --

CHAIRPERSON LUDERER: Thank you.

DR. SHEETS: -- and apology for running over time.

CHAIRPERSON LUDERER: Thank you.

Let's see, we have several more commenters. I believe Gary Roberts wished to comment. Jessica, do you have Dr. Roberts and can you unmute him?

MEETING MODERATOR: I sure do. All right. Let's see Dr. Roberts, I'm going to go ahead and unmute you and then go ahead and take yourself off self-mute as well.

MR. ROBERTS: Thank you. I presented my thoughts on imidacloprid previously alongside glyphosate. This does come within the scope of your procedure to defer to U.S. EPA as an authoritative body and I will not repeat those comments here.

Thank you for your time and consideration.

CHAIRPERSON LUDERER: Thank you.

All right. Let's see we have Daniel Minnema from Syngenta wanted to comment, I believe, on thiamethoxam. Jessica, do you have him and can you unmute him?

MEETING MODERATOR: Um-hmm.

CHAIRPERSON LUDERER: All right. Thank you.

MEETING MODERATOR: I see him as well. All right, I'm going to go ahead and unmute. And you are unmuted, so you can begin speaking.

DR. MINNEMA: Can you hear me?

MEETING MODERATOR: Yes.

CHAIRPERSON LUDERER: Yes.

DR. MINNEMA: Okay. I really don't have any comments. I just want to reemphasize the point that's been made that in these guideline studies, we use the very high dose levels. And usually, it's at those high dose levels that are associated with various toxicities that we see these effects. And that's also true for these reproductive studies, where the females -- or the dams are also affected in some cases very severely at the high dose levels. And the effects that we're seeing in the pups are very likely secondary to that and I'll leave it at that. Thank you. And thank you very much for taking the time. I appreciate it.

CHAIRPERSON LUDERER: Thank you.

And I believe our last commenter is Dr. Jennifer Sass from the Natural Resources Defense Council. And could -- is -- Jessica, do you have her on -- and could you please unmute her, if you do.

MEETING MODERATOR: Um-hmm, absolutely.

CHAIRPERSON LUDERER: Okay.

MEETING MODERATOR: All right. So I'm going to go ahead. You're unmuted and you can begin speaking.

DR. SASS: Thank you very much. So I'm with NRDC, the Natural Resources Defense Council. I also commented very quickly on glyphosate, but really most of my comments, which were submitted in writing too, so I hope that you have them, are on the neonicotinoid pesticides.

So I want to touch on the main points quickly for you. The first is that we're asking that the seed treatments also be included in the exposure evaluation, because we think that their roughly half of the neonic use in California and across the country. And we've presented some pretty carefully collected data from California databases to show that with some exact numbers.

We're asking the Committee to recommend that the use of neonics on seed treatments be collected and publicly disclosed. It's difficult to get this information, but it's important. And California has an opportunity to make this information publicly accessible, because it has the best pesticide tracking system in the country and a diverse agricultural industry, which means that a lot of the neonic use is used in California.

The second point we point out that studies that

fail to include metabolites may under predict exposure. For example, in the acetamiprid studies, it's the metabolites that had -- that showed -- were associated with the elevated risk of small for gestational age in the Ichikawa 2019 study that was in the prioritization report on page 80. And the original study by those authors concluded and -- at the end that their findings suggested that the need to examine potential neurodevelopmental toxicity of the neonicotinoids and metabolites in human fetuses. They really emphasized that in that 2019 study.

It was also highlighted in some data that isn't in your report, but that relates to drinking water. It was some studies in 2019 and earlier by USGS and University of Iowa collaborative researchers. And they showed that the metabolites in drinking water could actually be chlorinated with standards drinking water treatment and it was those chlorinated byproducts that were most toxic and that they were concerned about. Some of them were several hundred times more toxic than the parent compound. And they did find this in tap water in the University of Iowa. They took like samples from their lab.

So it is important and we suggest that the Committee recommend incorporating relevant studies that monitor neonic metabolites in biota, including water and

drinking water, and soil, as well as human biomonitoring. And recognize that not having those data may underestimate risks in the -- in studies.

We also want to point out that the industry-sponsored guideline studies that have been recommended by your industry speakers that preceded me often underestimate risks and that no effect results should be interpreted with caution. This is because the studies are designed to primarily look at standardized protocols and look at apical effects, like cancer organ weight changes, body weight changes, skeletal malformations, loss of fur, convulsions, death. But they -- these significant toxicity endpoints may miss a lot of the important kinds of things that you would expect from compounds like the neonic pesticides that act on neurological receptors to impair cholinesterase -- acetylcholine activity, especially during fetal or early life developments where you could have more chronic developmental effects.

So in short, we -- and I also pointed out some details in my comments of specific neonic guideline studies that I think were misreported or at least if you look only at the conclusions of those original studies, the conclusions say that there's no effects at mid or low doses, but, in fact, there are effects at the mid and low

doses. And some of them are statistically significant, but they might not be across all of the endpoints examined.

So I have some details in there. You should ask for those original -- the study summaries. They're called DERs, the data evaluation records, that EPA produces where this -- the scientists have generated those. In particular, there's a memo that I've cited in my own comments from the EPA statistical experts that have said they actually provided a corrected statistical analysis, that's what they call it, and used a more appropriate model, and appropriate statistical methods. And they did conclude that some of the effects at the low- and mid-dose were relevant and important, particularly the auditory startle reflex in male rats that were exposed prenatally at both the mid-doses as well as the high doses.

They sent that memo, but it did not get into the final report. It was passed through an EPA chair named Jess Rowland who has now come out in the glyphosate litigation as one of the people that was an EPA staff person working closely with Monsanto.

DIRECTOR ZEISE: Okay. Ulrike, I just want to flag that the five minute time limit has been passed.

DR. SASS: Okay. I'll just refer to my written comments. Thank you very much for your hard work. We

appreciate it.

CHAIRPERSON LUDERER: Thank you. And I believe that is the last of the public comments. Is there anyone else that -- that I've missed who wished to make a public comment?

COMMITTEE DISCUSSION AND RECOMMENDATION

CHAIRPERSON LUDERER: Okay. I think -- Dr. Sandy, I think you wanted to clarify something about the maternal toxicity question.

DR. SANDY: Yes. Thank you. I wanted to actually clarify three points. And the first one is maternal toxicity and what we say in our 2004 prioritization process document on page four, which you can refer to. We're talking about weighing the factors in prioritization, which is what we're doing now in animal studies. And we mentioned several things.

And we say, "In accordance with guidelines of the U.S. EPA, Environmental Protection Agency, adverse developmental effects that co-occur with maternal toxicity and reproductive effects that co-occur with systemic toxicity are considered evidence of reproductive toxicity, unless these toxicities are severe enough to preclude interpretation of the study". And this is in the context of prioritization.

The second clarifying comment is also referring

to page four of this prioritization process document that was sent to you. And it's cited in our report and it's from 2004. And this has to do with the authoritative body reviews that you've heard about a few times. So we do say, "It's unlikely that chemicals will be proposed for your Committee's review that have been recently reviewed by an authoritative body and found to have insufficient evidence of reproductive toxicity. Exceptions to this generalization may occur, for example, if an authoritative body has evaluated a chemical but failed to review all relevant data or compelling new data have become available since the evaluation". And I'll just point out that for these chemicals, there's a number of papers that are coming out last year, and this year, and the year before that.

I'll also make my third comment, which is about Proposition 65 is concerned with developmental effects. And in humans, we're concerned with exposures to humans before birth. I'll point out that many aspects of brain development in the early postnatal period in rodents correspond to the prenatal period in humans.

Thank you.

CHAIRPERSON LUDERER: Thank you, Dr. Sandy.

Do we have any additional discussion from the Committee on neonicotinoids?

Dr. Woodruff.

COMMITTEE MEMBER WOODRUFF: Yes. I -- I guess a follow-up with Dr. Sandy, but we also are concerned about male or female reproductive health endpoints independent of when the exposures occur, right? It doesn't have to be a developmental exposure.

DR. SANDY: That's correct. There are three different major endpoints that fall under reproductive toxicity in terms of Proposition 65, developmental toxicity, female reproductive toxicity, and male reproductive toxicity. And those latter two can occur with exposures after birth, of course.

COMMITTEE MEMBER WOODRUFF: Right, because I think I just want to clarify that some of the studies are exposures that occur during development, and some of the commenters talked about that. Studies that -- a lot of the studies that was looking at in terms of the male reproductive effects were exposures that occurred -- well, many of them were in adolescents or adults and had dose response information. So I just -- because I think I got kind of -- I was kind of getting confused from the commenters that there's different exposures and different outcomes.

And then I did also want to note that there was -- I heard saying that, yes, there is effects that

have been observed in these animal studies and also that there's variation in what those observations are. And I think that we are prioritizing. We're not doing an in-depth review of all the literature, and the pros and cons, and all that type of stuff. So that's what would happen should this Committee -- should these chemicals -- these chemicals be reviewed by OEHHA, and then come before the Committee, and then we would do something in depth. And it's -- given the literature that we have available, I think that this warrants concern. For some of them I agree that there is different groups of these. And, I mean, there's different -- there's four individual chemicals in here and thinking about having these prioritizing is important. I think the original conversation we had about usage is a good way to think about it.

CHAIRPERSON LUDERER: Okay. Thank you, Dr. Woodruff. Any additional comments?

So as a -- yes, Dr. Plopper.

COMMITTEE MEMBER PLOPPER: I just want to follow up on Dr. Woodruff's comments. I disagree with the comments by the commenters about the fact that there's no male reproductive toxicity. The most detailed studies we had available were for -- I will probably mispronounce, but imidacloprid. There's 11 studies on male

reproduction, six of them show testis formation, four of them show sperm loss. And the reason the others don't show it is because they didn't look. And the other thing that I think is of concern is that virtually all of those studies that looked, and that's about - what have I got here - nine of them, found that there was some evidence of severe -- severe oxidative stress in the testis.

So I just want to say that I -- I could not find in any of the literature we were provided any evidence that there was -- that male reproductive effects were not significant, because they were all -- they showed up regardless of what the study was. That's -- that's all I wanted to say to follow what she had just said. There -- we're looking at different issues than they are. We haven't -- I don't know how many of these are dose responses. But the fact that everybody is finding it and in some cases it's not a big deal of whether it's high dose, low dose, middle dose, I think -- and particularly when we're talking about four different species here of mammals. So I just -- that was all I wanted to say.

CHAIRPERSON LUDERER: Okay. Thank you.

Any other comments?

Dr. Baskin.

COMMITTEE MEMBER BASKIN: I've been enjoying the discussion and all the science and the comments. I think

if we're going to actually get anything done, I would make a motion that we vote to globally say this is a group of chemicals that we need to do further research, which doesn't mean that any of them are going to be listed. But if we're going to go chemical by chemical in each one these groups, I think that's going too be onerous. And if I'm not mistaken, the goal today was kind of to prioritize. So it doesn't mean that we're specifically saying one of the subchemicals in the group or, you know, one of the -- different variations is, you know, potentially dangerous. We're just saying that we're going to look at all of them carefully. Otherwise, I just don't know how we're going to get done.

CHAIRPERSON LUDERER: Perhaps the staff can clarify that. My understanding was that you wanted us to vote on each of these individually. Is it -- would it be possible to vote on them as a group?

COMMITTEE MEMBER BASKIN: Well, actually the staff -- I don't think the staff said that quite frankly. I think that was said by a number of people who were from industry.

CHAIRPERSON LUDERER: Dr. Sandy.

DR. SANDY: Yeah. Actually, we are asking you to vote on them individually. You're free to give us a recommendation on the group as well.

COMMITTEE MEMBER BASKIN: I think we should have listed them individually then.

DR. SANDY: They are. They are individual summaries. And we just grouped them for purposes of discussion. We thought there would be some efficiencies of scale in the discussion by the discussants.

COMMITTEE MEMBER BASKIN: Okay. Understood.

COMMITTEE MEMBER WOODRUFF: But can I then -- because I -- I totally hear what Larry is saying. I wonder if we should think about imidacloprid as a higher priority, because it's use is so much higher and then ask that the other ones kind of -- I don't know. I would recomm -- you can all vote. Of course, everyone votes the way they want, but we don't lose sight of the other ones. That's how I would -- how I think about them. I think we're going to run into the same when we get to the parabens and the PFAS as well, so...

CHAIRPERSON LUDERER: Yes. All right. Well --

COMMITTEE MEMBER WOODRUFF: So I thought that was a real question. I guess if I was going to prioritize them, I'd take it based on right now on use. And there are more studies on it, I mean, so -- but I --

CHAIRPERSON LUDERER: Okay.

COMMITTEE MEMBER WOODRUFF: You know, with that, I mean, we could get the BPA effect where it's like, well,

you just switch over to another one. So that's why I just feel like keeping an eye on the other ones is important.

CHAIRPERSON LUDERER: Well, so I suggest we go through them one by one and vote. And then we can also kind of make a recommendation to view -- to assess them as a group vote on both ways, if that's all right.

Okay. So why don't we start out with acetamiprid. So do I see any raised hands for high concern?

(No hands raised.)

CHAIRPERSON LUDERER: I do not.

Moderate priority?

(Hands raised.)

CHAIRPERSON LUDERER: Okay. Dr. Plopper, Dr. Woodruff, Dr. Hertz-Picciotto, Dr. Baskin, Dr. Carmichael, Dr. Auyeung-Kim, Dr. Allard. And did I say Dr. Breton raised her hand? Yes. Okay. Dr. Breton and Dr. Luderer.

Any for no concern?

(Hand raised.)

CHAIRPERSON LUDERER: Dr. Pessah. All right. I think that's everyone.

Okay. Moving on to clothianidin, high priority?

(No hand raised.)

CHAIRPERSON LUDERER: I don't see any hands.

Moderate priority?

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Woodruff, Dr. Plopper, Dr. Baskin, Dr. Carmichael, Dr. Auyeung-Kim, Dr. Allard,

All right. Do I see any -- and Dr. Luderer.

And low priority -- or no priority rather.

(Hand raised.)

CHAIRPERSON LUDERER: Dr. Pessah, Dr. Breton, and Dr. Hertz-Picciotto.

All right. Moving on to imidacloprid. High priority, and votes?

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Plopper, Dr. Woodruff, Dr. Carmichael, Dr. Allard, Dr. Luderer.

Okay. Moderate.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Baskin, Dr. Breton, Dr. Hertz-Picciotto, Dr. Auyeung-Kim. And, Dr. Pessah, did you have your hand raised?

No.

Or is that no priority, any votes on that for -- I think -- are you speaking? You might be. You're muted. Oh, okay. Low priority for imidacloprid, any votes for that?

Okay. I'm not sure if Dr. Pessah voted. Okay.

All right. We'll move on to the next is

thiamethoxam. All right. High priority.

(No hands raised.)

CHAIRPERSON LUDERER: I don't see any hands for high priority -- putting that in the high priority group.

Moderate priority.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Plopper, Dr. Woodruff, Dr. Carmichael, Dr. Allard, and Dr. Luderer.

Low priority.

No priority, sorry.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Baskin, Dr. Breton. Dr. Hertz-Picciotto, and Dr. Pessah, and Dr. Auyeung-Kim.

All right. So those are all the individual chemicals. Do we want to also vote on them as a group? We can go ahead and do that, since they're -- no. Dr. Baskin shakes his head. Okay.

All right.

COMMITTEE MEMBER WOODRUFF: Yeah. I think it's different than what we thought.

CHAIRPERSON LUDERER: Yeah. Yeah. Okay.

All right. I think now we do need to take a break, since it's been quite a while since we've had a break. So we'll schedule a 10-minute break, so it's 3:00 o'clock. So we will reconvene at 10 after 3:00. All

right. See you then.

(Off record: 3:00 p.m.)

(Thereupon a recess was taken.)

(On record: 3:10 p.m.)

CHAIRPERSON LUDERER: All right. Welcome back, everybody. I think we're all back and I think we need to start out by going back to Dr. Pessah, because I believe we didn't get your vote on imidacloprid I think that was the...

COMMITTEE MEMBER PESSAH: Moderate.

CHAIRPERSON LUDERER: Moderate. All right. Thank you.

PARABENS

COMMITTEE DISCUSSION

CHAIRPERSON LUDERER: Okay. Then we will next move on to parabens. Again, this and the next set of compounds, the PFASs, are -- we have groups of chemicals here. So I think we can have each discussant give their reviews for all of the members of those groups, even though we will at the end have to vote on them separately, just like we did for the neonicotinoid pesticides. So for the parabens the lead discussants are Dr. Baskin and I. Dr. Baskin, would you like to begin?

COMMITTEE MEMBER BASKIN: Sure. This may be a little less of an issue. So there's four parabens that we

were looking at. And in reviewing the literature, there was basically a low or no, which I guess is the same thing today, or in this meeting, evidence for really listing any of these compounds. I think the key -- some of the key data -- oh, let's see. I just lost my screen there.

Yeah. Some of the key data is -- our colleagues up north in 2020, so obviously contemporary Health Canada, they found no reasons for listing a number of the parabens. The major effect that we are seeing in some of the studies, in specifically male reproductive health, was looking at sperm analysis. And in a number of them, there was actually no difference, and then others, there were differences. But we've been seeing changes in sperm quality based on a number of World Health Organization studies over the years, but really no change in fertility.

So I didn't think that was actually quite relevant. There is one study that looked at specifically propyl paraben. That's if Fisher 20 study -- 2020 study, but there were so many confounding variables and measuring human anogenital distance has not proven to be the fifth vital sign. I think they're still fraught with multiple user issues.

So in summary, I did not find any evidence actually for any of the parabens for moderate or high evidence for listing. And that's my short and sweet

summary.

CHAIRPERSON LUDERER: All right. And that's based on epidemiological literature, correct?

COMMITTEE MEMBER BASKIN: Correct.

CHAIRPERSON LUDERER: Just to clarify that.

Okay. Thank you.

So for the parabens there, there were certainly a much larger number of animal studies in -- for the parabens than I think than there was epidemiological literature. So I'm going to try to go by that -- through them one by one.

So one thing that I do note for all of them in butyl paraben, the first one that I'll be talking about, is that they are in wide use, butyl paraben is an antimicrobial preservative used in cosmetics. There's more than 20,000 cosmetic products, as well as medications, suspensions, drugs and foods.

In the animal studies, I thought that there was good evidence in the -- with the prenatal and postnatal exposure where there were neurobehavioral deficits in learning, social and memory behaviors noted, as well as reduced anogenital distance in males and females, increased mammary gland growth in females, decreased ovary weight, impaired steroidogenesis, and ovarian folliculogenesis, and subfertility also in females.

And in males, there were -- was noted with prenatal and postnatal exposure combined, decreased testicular descent, decreased sperm counts, and motility -- sperm motile, as well as abnormal morphology of the sperm.

There were not as many findings for female reproductive effects. There was myometrial hypertrophy noted and increased uterine weight in a uterotrophic assay, but that latter finding was not consistent.

Regarding male reproductive effects, there were, by several routes of exposure noted, high oral doses, dietary, and subcutaneous injection, histopathological abnormalities in the testes, abnormal sperm morphology in multiple studies, and additional de -- with starting at prepubertal ages for mice. Oral dosing through the diet was associated with decreased round and elongated spermatids, and decreased elongated in rats, and decreased elongated spermatids in mice, as well as epididymal and testicular sperm counts decreased in -- in rats and mice.

Moving on to isobutyl paraben, this has similar uses as butyl paraben, but there was much -- there are much less data on isobutyl paraben. But interestingly, again under the reproductive effects, there was myometrial hypertrophy and an increased uterine weight noted in a uterotrophic assay in females.

And in -- with prenatal and postnatal exposure, there was increased notice changes in the uteri as well with increased uterine weight and uterine sensitivity to estradiol. But in contrast to the butyl paraben, there weren't effects noted on anogenital distance or on epididymal sperm counts in motility.

For methyl paraben, again similar uses as the other two, with about 12 -- according to the document, about 12,000 cosmetic products, many -- the majority of which, more than 9,000, are leave on products containing this paraben. There -- in the animal studies, there was -- there were quite a few studies looking at female reproductive effects showing morphological and histological changes in the mammary glands with pre -- peri- or postnatal exposure. With adult exposure, there were effects noted on the estrous cycle with increased diestrus phase, time in the diestrus phase, and increased expression of several genes anti-Müllerian hormones, steroidogenic acute regulatory protein, and cytochrome P450 11A1 and primordial follicles, and increased FSH levels and decreased total number of follicles. There was also delayed vaginal opening, which is an indicator of sexual maturation and decreased estrous cycle length with prepubertal exposure.

And in gerbils, there was also noted epithelial

hyperplasia, increased androgen receptor positive cells, stromal inflammation and intraepithelial neoplasia in the Skene's which are the female counterpart to the prostate gland.

Interestingly, in male reproductive effects, there were no effects noted in two studies on, you know, organ weights and sperm parameters. However, again, in a gerbil study, there were morphological changes in the prostate, akin to what had been noted in the Skene's periurethral glands in the females, including epithelial hyperplasia, increased proliferation and increased androgen receptor protein expression.

Finally, moving to the last paraben, propyl paraben. This occurs naturally in many plants and is also synthesized for use in cosmetics and pharmaceuticals. So similar uses as the other parabens. Again, 9,000 cosmetics were listed by the FDA that contain propyl paraben, of which 7,500 were leave on. And this -- there was a not very large database for propyl paraben. The -- there was some female reproductive effects noted. Again, alterations and expression of anti-Müllerian hormone in the primordial follicles with adult exposure, and increase serum FSH levels and decreased total number of follicles with adult exposure in rats. And prepubertal exposure in rats also caused myometrial hypertrophy, but really very

limited for propyl paraben.

So as far as my -- I would rank butyl paraben high priority, isobutyl paraben as moderate, methyl paraben as high, propyl paraben as moderate.

Okay. Thank you. And we'll open it up for discussion by the Committee, any comments?

All right. No comments. We have, I believe, at least one public.

COMMITTEE MEMBER WOODRUFF: Chair.

CHAIRPERSON LUDERER: Oh. Yes.

COMMITTEE MEMBER WOODRUFF: I thought -- I noticed that OEHHA didn't have any coverage of the biomonitoring data, but -- is it because there's no data from California. My understanding is there's pretty widespread exposure to these parabens, because they're high --

CHAIRPERSON LUDERER: Yes. Because of the products that they're in, that's correct.

COMMITTEE MEMBER WOODRUFF: Right.

CHAIRPERSON LUDERER: Yeah. Does -- any comment from the staff on that?

COMMITTEE MEMBER WOODRUFF: I also want to ask you a question, Ulrike, but -- okay. I'll wait.

CHAIRPERSON LUDERER: Okay.

DR. SANDY: We -- that's just something we didn't

add to these compounds.

COMMITTEE MEMBER WOODRUFF: Okay.

DR. SANDY: We had the information on how often they're used in different products, but we apologize. We didn't include the biomonitoring data.

COMMITTEE MEMBER WOODRUFF: Okay. I mean, I just -- Ulrike, did you note any of the -- I know that there's been some in vitro studies of these parabens, right? Because they're looking at their --

CHAIRPERSON LUDERER: Oh, actually, thank you for reminding me, because one of the things I did want to comment on is their relative potency for binding to the estrogen receptor alpha and beta. So it's -- the order of potency for that is that the greatest binding affinity is the butyl paraben -- isobutyl paraben, the butyl -- then followed by butyl, isopropyl, propyl, and ethyl.

So to some extent, the -- you know, I wouldn't say that -- I think -- I wouldn't say that the effects that we're seeing necessarily followed that rank order, partly because there's such a difference in the numbers of studies available for each of the parabens. So I think that's, you know, difficult to rank them that way.

There's other studies that also showed activation of PXR and CAR by these compounds in, let's see, in MCF-7 cells, as well as rat cells, and increased estrogen

receptor dependent transcription of reporter genes by both butyl paraben and its metabolite as getting back -- getting to your question about the mechanistic effects.

And let's see, similar results were noted with isobutyl paraben with the increased estrogen receptor transcriptional activity and CAR activation.

So those were the two for which there was the most of those types of mechanistic data.

COMMITTEE MEMBER WOODRUFF: All right. Thank you.

CHAIRPERSON LUDERER: Um-hmm.

Okay. Any other discussion?

PUBLIC COMMENTS

CHAIRPERSON LUDERER: All right. So we do have a public comment, at least one. I'm not sure if we've gotten any others. But we have a comment from George Daston from Personal Care Products Council. Did we get any additional requests for public comment on the parabens?

Okay. So, Jessica, if you have Doc -- if you can unmute Dr. Daston, assuming he is on the line.

MEETING MODERATOR: Absolutely. He's here.

CHAIRPERSON LUDERER: All right. Thank you.

MEETING MODERATOR: Doctor, I'm going to go ahead -- you're welcome. I'm going to go ahead and unmute

you now and you can begin speaking.

DR. DASTON: Okay. Thanks very much. My name is George Daston. I'm a toxicologist with Procter and Gamble. I'm here at the behest of two trade associations, Personal Care Products Council and Consumer Healthcare Products Association.

I know many of you both on the Committee and on staff. And it's good to see your faces. For those of you I don't know, just a brief introduction. I've been engaged in research in developmental and reproductive toxicology since the 1970s. I'm a past president of the Teratology Society and President of Society of Toxicology. Also, like you, I've done volunteer advisory work for the State of California, in my case it's for their Green Ribbon Science Advisory Panel.

What I hope to do in my few minutes here is just talk about all of the parabens at once and really try and convince you that they are moderate to no priority chemicals.

There's three things I want to touch on: mode of action, metabolism, and in vivo effects. In terms of mode of action, Ulrike has already discussed the mode of action as being estrogen receptor interaction and agonism. These compounds are weak. They range from about 10,000 to 100,000 times less potent than 17 beta-estradiol for the

butyl parabens to about a million times less potent for methylparaben.

There's some evidence in the literature that they are also anti-androgenic, but those -- that's controversial. These studies are easy to do, so they're also easy to do poorly. Looking at the studies that are done with high quality control, particularly the EPA's ToxCast data set, there's no indication of anti-androgenic effect in over a dozen assays, but there is evidence of the estrogenic effect.

So, of course, there is reason for concern. Now, why doesn't that translate into significant effects in vivo? And the reason is metabolism. These compounds are all esters of para-hydroxybenzoic acid. And there are esterases at all portals of entry, whether the skin, GI tract, whatever for which these parabens are extremely good substrates.

There have been good human studies looking at the level of parabens after dermal application, so Janua et al., showing that even with heroic amounts of parabens administered with two phthalates that would be competers for the esterase activity, they're still less than 0.1 percent of the para -- of the butyl paraben that gets through the skin in tact.

So that really explains why both in humans we

don't see effects. And in animal studies, there's this real disconnect between effects -- between studies that are done by the subcutaneous route that bypasses the first pass metabolism and studies that are done by either the oral route, where there is first pass metabolism, or dermal route.

When we look at those studies again, you know, there's a lot of variability in how the -- in the outcome of the studies. But in the studies that have GLP, higher statistical power, there tend to be fewer effects. With methyl paraben, you know, there's really nothing to write home about. With butyl paraben, there are some controversies of a study by Boberg in 2016 showed effects on epididymal sperm concentration, which is consistent with an anti-estrogenic effect, or I'm sorry, an estrogenic effect, but there's no dose responsiveness. And all of the sperm count data are smack dab in the middle of the historical control range from the controls that are higher, and studies with similar study designs, like Hoberman et al. saw nothing even at higher doses.

So it doesn't seem as though, you know, these are studies -- it doesn't see as those these are compounds that have tremendous potential for human reproductive toxicity.

I'll just end with something that isn't part of

your remit, but that I think about, which is these parabens are preservatives. Preservatives do perform a useful function for public health, in terms of preventing microbial contamination of products that could then make people sick. And there -- the -- there aren't a lot of preservatives that are without baggage. And the parabens are among the safer ones. If we swap them out, we'd be swapping out fairly safe things for either sensitizers or formaldehyde generators.

So I know that that's not, you know, part of the DART Committee's remit, but it's something that I think about from a public health standpoint.

So I thank you for your time.

CHAIRPERSON LUDERER: Thank you very much.

COMMITTEE DISCUSSION AND RECOMMENDATION

CHAIRPERSON LUDERER: All right. Do we have any additional discussion or comments by the Committee before we move on to our vote?

All right. So we'll -- we will go through these compounds one by one and vote for each of them separately. So starting with butyl paraben, so raise your hand if you have high -- rank this as a high priority.

(Hand raised.)

CHAIRPERSON LUDERER: Okay. Luderer, one.

Moderate priority.

(Hands raised.)

CHAIRPERSON LUDERER: Woodruff, Allard, Plopper, Baskin, I believe Pessah, yes, Breton, Carmichael, Auyeung-Kim. Did I get anyone wrong?

Okay. And so then nobody was voting -- Did anyone want to vote no priority?

No. Okay.

All right. Moving on to isobutyl paraben, high priority.

DIRECTOR ZEISE: Pardon -- pardon me. Pardon me, Ulrike. So I think Dr. Pessah, did you want to vote no priority on the --

COMMITTEE MEMBER PESSAH: My vote was no priority, yeah.

CHAIRPERSON LUDERER: Oh. Okay. I thought you had your hand raised for moderate. Sorry.

COMMITTEE MEMBER PESSAH: I was going like this.

(Laughter.)

CHAIRPERSON LUDERER: Okay. All right.

DIRECTOR ZEISE: And, you know, maybe we can also as we finish, Ulrike, if you wouldn't mind just summarizing the vote, that would be great.

CHAIRPERSON LUDERER: Okay. I'll try to do that.

DIRECTOR ZEISE: Yeah, thanks.

CHAIRPERSON LUDERER: All right. That means I

need to write them down. All right. So let's start with isobutyl paraben. Anyone vote for high priority.

(No hands raised.)

CHAIRPERSON LUDERER: All right. I don't see any hands raised for high priority.

Moderate.

(No hands raised.)

CHAIRPERSON LUDERER: No votes for moderate priority.

Low priority, then I assume carries the day on that one.

(Hands raised.)

CHAIRPERSON LUDERER: Okay. Thank you. So all the Committee members voted low priority on that -- on isobutyl paraben.

Methylparaben, high priority.

(No hands raised.)

CHAIRPERSON LUDERER: Moderate priority.

(Hands raised.)

CHAIRPERSON LUDERER: Okay. I see Dr. Carmichael, Dr. Allard, Hertz-Picciotto, Dr. Plopper, and Dr. Woodruff, and Dr. Luderer, moderate.

So low priority?

(Hands raise.)

CHAIRPERSON LUDERER: Dr. Baskin, Dr.

Auyeung-Kim, Dr. Breton. Did we get Dr. Pessah's vote on that one?

Is that low priority -- or no priority? I think your connection may not be very good.

(Laughter.)

CHAIRPERSON LUDERER: Methyl paraben, was that no priority, Dr. Pessah?

COMMITTEE MEMBER PESSAH: It was low priority.

CHAIRPERSON LUDERER: Yeah, or -- okay. All right. Okay. Sorry, did we get all those then, everyone? We got all your votes. I think we did.

I didn't write them down. I'm sorry. Do I need to go through them again, Dr. Zeise?

DIRECTOR ZEISE: We've captured them. Thank you.

CHAIRPERSON LUDERER: Okay. Wonderful. Thank you

Okay. The last one is propyl paraben, high priority.

(No hands raised.)

CHAIRPERSON LUDERER: Zero. Nobody is voting high priority on that one.

Moderate priority for propyl paraben?

(No hands raised.)

CHAIRPERSON LUDERER: Dr. Woodruff is your -- is your hand raised? No.

Okay. All right. And no priority.

(Hands raised.)

CHAIRPERSON LUDERER: Okay. Okay. Everyone is voting no priority on that one.

Okay. So we have completed all the parabens.

DIRECTOR ZEISE: Okay. And that's including you, Dr. Luderer?

CHAIRPERSON LUDERER: Yes. Yes.

PFAS

COMMITTEE DISCUSSON AND RECOMMENDATION

CHAIRPERSON LUDERER: All right. Okay. Then moving on to the PFASs. Our discussants for the PFASs are Dr. Allard, Dr. Breton and Dr. Hertz-Picciotto so shall we start with Dr. Allard.

COMMITTEE MEMBER ALLARD: Sure. I'm actually going to -- I mean, I'll go a little bit more in detail, but I'm going to start with just general comments about at least the ones that we had to review, which is that they are on the long chain side of the PFAS species. And so therefore, their half-lives are just ridiculously long. We're talking about in humans several years, in animal models, many months, for all of them.

There's, of course, some granularity. So I mean the studies change a little bit, but PFNA, one of the four, probably had one of the shortest half-lives. And I

think PFUnDA had one of the longest half-lives. But again, we're still talking about many years. So I think PFNA, the shortest that's been measured in humans is 2.5 years, and PFUnDA I think is like seven, if I'm correct. Actually, sorry, PFHxS has been measured all the way up to 15.5 years in some studies. So just right there that raised the bar at the very minimum, at a medium, in terms of needing to look at these longer chain PFASs.

Then, of course, there's the layer of, you know, what data do we already have on those chemicals? And I'll just, I guess, summarize the trove of data saying that PFDA from my -- through my lens PFDA and PFNA had some -- some concerning reproductive data in animal models as well as in vitro data, especially with the association with PPAR-alpha. Actually, the PPAR-alpha agonist that definitely put them in the high category for me, so that's PFDA and PFNA. And then, PFHxS, and PFUnDA had less data. And so that put them in the -- for me, in the medium category. There was actually a paucity of data on -- I thought on these two of some of the studies that are looked at were not, you know, low powered and not looking at -- I'm thinking of the PFA -- my God -- PFHxS chemical that had a really interesting study on germ cell tumors, for example, but that was only 84 in total. So it was not necessarily very high powered.

So -- so, yes, for me, the main driver and really the clear cause for concern is that really long half-life in humans for these longer chain PFASs.

CHAIRPERSON LUDERER: Thank you, Dr. Allard.

Dr. Breton.

COMMITTEE MEMBER BRETON: Okay. So, okay, overall -- so I did initially think about these much more as a group than individually. And as a group, certainly, I would agree with Dr. Allard that -- that this gives me -- this is a high priority for me. I would rank them as a high priority as a group.

Something to mention is that two of the PFAS -- PFOS and PFOA have actually already been listed under Prop 65, so -- from the same family.

With regard to the individual source -- to summarize the individual chemicals, I'll start with PFDA. And this is -- these are the epi studies that I'm talking about. I would say -- so for PFDA, there's a lot of literature, you know, on -- on this one at this point. The evidence for associations with reduced fetal and childhood growth and for endocrine disruption are both compelling.

So there are about five studies looking at growth metrics all showing association -- significant associations. And these come from studies that have large

sample sizes in general and are in diverse international cohorts. Although, I'll note that none of them are from the U.S.

There are also three studies showing associations with thyroid hormones, you know, and a total of eight studies with generally moderate to large sample sizes that are looking at endocrine disruption across multiple countries. And I think the animal studies, though I didn't look at those as in depth, generally support some of these findings in humans.

For PFHxS, there is perhaps a little bit less data, but still quite a few studies. And the evidence is suggestive for the same endocrine and reproductive -- endocrine effects and also for reproductive effects in males and females. So there are -- there were at least four studies that showed positive associations, but they were looking at different hormones.

And so, you know, they weren't completely reproducible, because they were looking at different outcomes. And again, three to four studies looking at reproductive effects.

I would say there's a little bit less or more limited evidence for reduced fetal growth and metabolic effects for this particular chemical, so the literature is a bit more mixed.

For PFNA, the -- there -- the evidence for fetal growth is again sort of suggestive or even, I would say, compelling. Five studies showed inverse associations with birth weight, some had sex-specific effects, some did not. And I've -- there was one that showed no association with fetal biometry. There is also suggestive effects for neurodevelopment, for endocrine effects and for reproductive effects.

The literature is mixed in the sense that, you know, they're looking at different outcomes in these categories. They're not all looking at the exact same thing, but the -- so -- and then there were some limited effects looking at things like puberty, and respiratory health, and metabolic effects in the children.

And then for PFUnDA, this one had the least amount of evidence. There -- there are still four studies looking at endocrine effects again with thyroid hormones that are consistent. The other four studies -- four or five studies that looked at fetal growth, showing suggestive effects in line with some of the other ones in the family, and some more limited effects looking at neurodevelopment or in one -- in a couple cases asthma and eczema.

So that -- yeah, that's my summary of sort of each of the individual chemicals. I would say for me

individually, I would rate, you know, most of them high, with -- I would probably put the last one PFUnDA as moderate, if I were looking at them individually.

CHAIRPERSON LUDERER: Thank you very much for that summary.

Dr. Hertz-Picciotto.

You're muted I believe.

Still can't hear you.

COMMITTEE MEMBER HERTZ-PICCIOTTO: I'm sorry. I kept pressing it and it wasn't working. And then finally, it -- on the fifth try, it did, so...

(Laughter.)

COMMITTEE MEMBER HERTZ0PICCIOTTO: Yeah. So, Dr. Breton, did an excellent job of covering all of them. I actually spent a lot of time trying to figure out -- because in the beginning, I went through, you know, all these papers, a lot of papers, and it seemed like -- it was pretty clear that the PFNA and the PFDA, you know, those two were very clear right from the beginning, I guess because I started with the perinatal reproductive, you know, birth weight, birth growth, you know, length and all of those first.

And for those, the two others, the hexane sulfonate and the undecanoic acid, there seemed to be less as I -- as I went through it. And, in fact, I think it

was the PFHxS that actually showed some -- it appeared to have benefits, like it -- and there's study where it showed the decreasing percent a preterm births. And then there's another one that had its -- I think it was associated with higher -- I'm not finding that. But in any case, it -- I started out, and there were studies where it didn't show up.

You did catch that none of those were in the U.S., which I didn't even notice. But, in deed, you know, there's, you know, actually 11 studies of low birth weight, and small for gestational age, and length, and preterm delivery. And in the beginning, I was thinking that okay, well, PFHxS, you know, in several studies, seemed to actually be beneficial and that we would really need to separate these all out. So that's -- so that -- that still stands I think for the perinatal.

When I got to the neurodevelopment though, it -- it sort of -- in fact, the PF -- all -- well, definitely the PFHxS does show some of these neurodevelopmental effects, particularly this -- you know, one of these instruments that we use in a lot of studies called the Strengths and Difficulties Questionnaire that -- that comes up with the -- with findings and that include PFHxS.

There's fewer studies, you know, of neurodevelopment, but it starts to look like that when it

comes in. But then there are -- as Dr. Breton pointed out, there are much fewer studies. There are some studies showing no association with at least one study showing no association that did look at the undecanoic acid in the neurodevelopment.

However, I think really, in some ways, the strongest evidence in terms of these other two does come in when we start looking at the endocrine effects. And that's where the PFHxS actually does show thyroid -- there's multiple, multiple studies looking at thyroid hormones. And I think that the -- that's -- that's a place that we're really seeing -- and again, the fourth one, the less well studied one, which at one point I was thinking, oh, you know, there's just not -- not enough data here at all, but in fact it does show up for endocrine effects on several studies, and -- at least four studies.

And one of them actually was looking -- sorry not at thyroid, but at 450 aromatase. So -- and then there's several other studies looking at the sex steroids as well. So that's, I think, the place where I started to think, okay, maybe -- maybe all of them.

And then the final group were the reproductive ones. And there's several studies looking at, for example, irregular menstrual cycles and premature ovarian

insufficiency. And PFHxS shows up here. Although, they're one of -- in one place it's kind of a U shape. It's seems like both low and high levels of PFHxS, which is a little odd, because I don't think of it is an essential -- an essential compound in any way. But irregular menstrual cycles definitely for PFHxS. So for the other two -- another subcategory under the reproductive.

The male reproductive, there isn't that much. And then there's a few studies on these other DART effects here, metabolic effects, where there's a study of PFHxS showing a double -- a strong increase in triglycerides which seems to be of concern.

So, you know, all in all, I think -- you know, I started out thinking we needed to separate them out, and if we do, I think that they are -- they are different in terms of their impacts. But given the number of different things that DARTIC covers, including these perinatal, neurodevelopmental, endocrine, and the, you know, reproductive effects -- I mean, adult reproductive effects, I think that there's good reason to consider all of these at least medium, and I -- I would say high. This is a proliferating chemical that is on the rise, these chemicals, and -- the persistence that Dr. Allard point -- pointed out really these are -- these are -- these remind

me now of the organochlorines, which have left such a long legacy of toxicity of all kinds. And I would -- I would put these all in the high category at this point.

CHAIRPERSON LUDERER: Okay. Thank you very much.

Do we have any discussion about the PFASs?

Dr. Allard.

COMMITTEE MEMBER ALLARD: Yeah. I guess I want to point out that when we think about endocrine, or at least nuclear hormone receptors, we often think in sort of traditional terms of, you know, estrogenic or androgenic. But something that I was surprised was unmentioned, or maybe I missed it, in the document about this PFAS is that the fact that - and I mentioned it briefly - they are supposed to -- or many of them act as PPAR-alpha agonists. And it's unclear whether they could potentially associate with other PPARs.

And several of the data mentioned in -- the pieces of data mentioned in the document for several of these chemicals actually really point in that direction. For example, for PFNA, there was one study that mentioned how there was lipid droplet accumulation as early as the pre-implementation embryo, really for me, you know, suggestive that things go awry from very, very early on with regulation of this really important part of metabolism.

So although there's some -- there's -- for some of them, there's not necessarily a ton of data out there. The fact that some of those pieces of data really align well with what we understand, I think pretty solidly at the mechanistic level, is really concerning.

That's all I want to say.

CHAIRPERSON LUDERER: Thank you for that comment.

Any other discussion?

All right. We can then move on to the vote.

Again, we're going to -- to vote on them one by one. So we have PFDA first and who -- raise your if you would vote for that to be in the high priority category?

(Hands raised.)

CHAIRPERSON LUDERER: Okay. Dr. Auyeung-Kim, Dr. Carmichael, Dr. Breton, Dr. Baskin, Dr. Plopper, Dr. Allard, Dr. Hertz-Picciotto, Dr. Woodruff, Dr. Pessah, and Dr. Luderer. Okay. So that's unanimous.

Next is PFHxS. So for high priority, please raise your hand.

(Hands raised.)

CHAIRPERSON LUDERER: Okay. Dr. Breton, Dr. Baskin, Dr. Plopper, Dr. Hertz-Picciotto, Dr. Woodruff, Dr. Pessah. All right. And Dr. Luderer.

Moderate priority.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Auyeung-Kim, Dr. Carmichael, and Dr. Allard.

Okay. So then nobody is voting no priority for that.

DF --

DIRECTOR ZEISE: Summarize on that one, Ulrike, because -- Dr. Luderer I heard 7 highs and 3 moderates.

CHAIRPERSON LUDERER: Yes.

DIRECTOR ZEISE: Great.

CHAIRPERSON LUDERER: Okay. We're moving on to PFNA. For high priority, please raised your hands.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Auyeung-Kim, Dr. Carmichael, Dr. Breton, Dr. Baskin, Dr. Plopper, Dr. Allard, Dr. Hertz-Picciotto, Dr. Woodruff, and Dr. Pessah, and Dr. Luderer. So that's unanimous for high.

And PFUnDA, raise your hands for high priority. Anyone voting for high priority?

(Hand raised.)

CHAIRPERSON LUDERER: Dr. Pessah.

And moderate priority?

COMMITTEE MEMBER BRETON: I think he was frozen.

CHAIRPERSON LUDERER: Oh, he was? Okay. All right. We're having problems with that. Okay.

(Laughter.)

CHAIRPERSON LUDERER: Dr. -- all right, Dr. Pessah, you were not voting for high priorITY for PFUnDA, is that correct?

COMMITTEE MEMBER PESSAH: (Shakes head.)

CHAIRPERSON LUDERER: No. Okay. All right.

So no votes for high.

All right. So then moderate. Let's start again, please.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Auyeung-Kim, Dr. Carmichael, Dr. Breton, Dr. Baskin, Dr. Plopper, Dr. Allard, Dr. Hertz-Picciotto, Dr. Woodruff, Dr. Pessah, and Dr. Luderer. So that's unanimous for moderate on that one.

(Laughter.)

CHAIRPERSON LUDERER: All right. Okay. Thank you.

TITANIUM DIOXIDE

COMMITTEE DISCUSSION

CHAIRPERSON LUDERER: So now we're moving on to the titanium dioxide nanoparticles. The lead discussants are Diana Auyeung-Kim and I. So, Dr. Auyeung-Kim, would you like to begin?

COMMITTEE MEMBER AUYEUNG-KIM: Sure, I can begin. So titanium dioxide is widely used in consumer products

similar to benzophenone-3 that we discussed earlier. Titanium dioxide is commonly used in sunscreen at the end.

But unlike benzophenone-3, the FDA considers titanium dioxide as generally regarded as safe and -- safe and effective. FDA has indicated that the transdermal absorption of titanium dioxide nanoparticles confirm that the skin is a relative effective barrier to the penetration of titanium dioxide, regardless of the particle size, including those on the nanoscale.

And Australia's Goods Administrations also recently reached a similar conclusion. However, there are concerns about potential exposure to titanium dioxide through inhalation ingestion and also within nanoparticles formulation.

So there were no epidemiologic studies that were available to discuss. The maternal and developmental studies in animals were conducted in rat, mice, and monkey. These studies were conducted on titanium dioxide particle -- of very particle -- varying particle sizes. In the rat studies, there was no maternal or developmental toxicity. In the mouse, there were developmental toxicities that were a result of maternal toxicity and are placental effects. The monkeys -- oh, and the rat study was conducted in a GLP laboratory, but was not within the scope of GLPs.

The monkey study was not designed to determine if there were developmental effects and that used a non-relevant dose route -- intradermal dose route in a small number of animals. So there's no clear develop -- so there's no clear evidence of developmental toxicity.

However, there are indications of potential neurodevelopmental effects observed in rats and mice when exposed in utero. This -- which impacted the learning and memory in rats and mice, and changes in the physical out -- physical structure of the brain in the mice.

Additionally, titanium dioxide exposure reduced the levels of testosterone in multiple studies in rats and mice, which affected spermatogenesis, but there was no study conducted to look if there was an effect on fertility.

With the wide spread use and potential neurodevelopmental and male reproductive effects similar to benzophenone, I would say that it's high priority. However, you know, if we need to look at all the chemi -- the chemicals in totality and try and prioritize them that are on the list, I would say that this has a lower priority than benzophenone, because it is generally regarded safe and effective by the FDA.

CHAIRPERSON LUDERER: Okay. Thank you very much. I agree with most of what's been said that the

neurodevelopmental and the male reproductive effects I thought were the -- there was -- the evidence was most compelling in those two areas for titanium dioxide nanoparticles.

Also, with the -- with the developmental, I agree there was not much on developmental effects. How there was -- however, there was evidence for impaired placental vascularization and decreased placental weights in mice and rats, so as a -- as a maternal or reproductive effect.

So I agree, given the high exposure to these nanoparticles that because of the widespread exposure, I also would place it in the high priority category. And -- but I do agree that the -- the benzo -- that I would probably prioritize it lower than benzophenone-3 as well.

Any other comments on this compound?

Dr. Woodruff.

COMMITTEE MEMBER WOODRUFF: Yeah, I have a question. This is -- maybe Cal EPA can answer this for in nanoparticle, right?

CHAIRPERSON LUDERER: Yes.

COMMITTEE MEMBER WOODRUFF: This could be that the non-nano -- there's -- whatever there's -- it might not be toxic. Is that -- is that part of the feature of this one?

CHAIRPERSON LUDERER: Nanoparticle only, yes. So

it's specifically nanoparticles, so not larger.

COMMITTEE MEMBER WOODRUFF: Right. But was it -- was it your sense that the -- that that was in part one of the concerns about it was the structure of it?

CHAIRPERSON LUDERER: Yes.

COMMITTEE MEMBER WOODRUFF: Okay.

CHAIRPERSON LUDERER: Um-hmm, yes.

COMMITTEE MEMBER WOODRUFF: I had to ask it several times though to get it right, so thank you.

CHAIRPERSON LUDERER: Yeah. Dr. Plopper, did you have your hand raised?

COMMITTEE MEMBER PLOPPER: Yes. We're only talking about it as a nanoparticle in a compound, right, not something that's aerosolized?

CHAIRPERSON LUDERER: Well, the --

COMMITTEE MEMBER PLOPPER: Is that correct?

CHAIRPERSON LUDERER: I mean, there were -- the studies were inhalation as well as oral exposure, yes.

COMMITTEE MEMBER PLOPPER: Okay.

CHAIRPERSON LUDERER: So -- yes, so it could be aerosolized as well.

Any other -- and I'm not sure if it's used in any spray-on products. I don't think that the sun -- sunscreens do come in spray on formulation, so that would be and interesting question, whether that's a potential

route of exposure.

Dr. Woodruff.

COMMITTEE MEMBER WOODRUFF: But it could be -- the aerosol could be an occupational concern, right?

CHAIRPERSON LUDERER: Yes, occupation. Yeah, I was just thinking in terms of the widespread population exposure.

COMMITTEE MEMBER WOODRUFF: Right.

CHAIRPERSON LUDERER: Dr. Sandy.

DR. SANDY: Yeah, I can confirm that it has been used in spray-on sunscreens the titanium dioxide nanoparticles.

CHAIRPERSON LUDERER: All right. Thank you.

PUBLIC COMMENTS

CHAIRPERSON LUDERER: I guess -- all right. I don't believe we have any public comments on this, is that correct, Jessica? Did we -- or did we get any requests for public comment?

MEETING MODERATOR: Let's see, I'm looking at the --

MR. LEICHTY: We do have a request.

CHAIRPERSON LUDERER: We do. All right.

MR. LEICHTY: And it is from Stewart Averett on behalf of -- I'll let him say.

MEETING MODERATOR: All right. I do see that

name listed. So I'm going to go ahead and unmute. And on your side, you should be able to unmute yourself to speak.

MR. AVERETT: Thank You very much. I appreciate it. My name is Stewart Averett. And at this late hour, my brother Devron Averett, Dr. Devron Averett was going to present. We have also presented in writing before. He has communication limitations. He can't do this, but I do have a statement that he was going to make. It will be brief, of course, in lieu of your precious time.

So we appreciate the opportunity to offer comments and thank the Committee for its consideration. My brother's background, Dr. Averett's background, is that of a long-term pharmaceutical research and development laboratory worker and executive resulting in FDA-approved drugs, and dozens of peer-reviewed papers, and issued patents. So we are -- we are together presently interested in improving plant protection with safer agents.

As a general matter, the guideline study reference list on titanium dioxide nanoparticles it's useful. Within it, reviews and larger studies are likely to provide more powerful and relevant information and nuanced as well on the subjects of reproductive and developmental toxicology. There are reports also including from small studies and that -- or consider

molecular components as observed phenomena. This fact is observable in the references provided and I would like to take -- to call attention to the fact that the large toxicological studies have been conducted that indicate minimal risk. For example, the report of Warheit et al. is worth review in that literature list.

A key point regarding this material, titanium dioxide nanoparticles, is that it is not soluble or absorbed. And this, in fact, contributes to the persistent irritation of the respiratory tract that underpins the inflammatory response that we see with this agent, as well as other poorly soluble, low toxicity materials, or as you are probably familiar with from this, PSLT in parlance of NIOSH.

We note that one of the reviews listed in the reference suggests that systemic inflammation is problematic for DART, but that this finding is not related to the chemical nanoparticle titanium dioxide but rather is associated with any number of PSLTs, that is poorly soluble low toxicity materials.

So for the purposes of brevity, we note in particular that generalized inflammatory reactions as occur with high dose pulmonary exposure of any fine particulate that is not definitive to just titanium dioxide may, in fact, underpin most of the DART

observations that strongly indicates that there is not a rationale for a specific prioritization of titanium dioxide nanoparticles, but rather an observation that all fine particulates should be considered as a class.

And thank you very much for your time and all your efforts on behalf of California.

COMMITTEE DISCUSSION AND RECOMMENDATION

CHAIRPERSON LUDERER: Thank you for that comment. I don't believe we have any other comments. Do we have any further discussion by the Committee?

All right. Then we can move on to our recommendation. So again, please raise your hand if you feel that this should be in the high priority category, titanium dioxide nanoparticles specifically.

CHIEF COUNSEL MONAHAN CUMMINGS: Dr. Luderer, I think that Dr. Woodruff wanted to make a comment.

CHAIRPERSON LUDERER: Oh, I'm sorry. Dr. Woodruff.

COMMITTEE MEMBER WOODRUFF: Well, I just was going to remark on your comment about -- well, both of the comments, that it was -- that it could be high, but behind benzophenone-3 I don't even know if that's categorized, but that was how I --

CHAIRPERSON LUDERER: Yeah.

COMMITTEE MEMBER WOODRUFF: Yeah, I don't know if

that's a category, but that's what I was -- just wanted you to reflect on that a little bit more.

CHAIRPERSON LUDERER: Yeah. You mean, why? I think --

COMMITTEE MEMBER WOODRUFF: (Inaudible.)

CHAIRPERSON LUDERER: -- there's a much larger database --

COMMITTEE MEMBER WOODRUFF: -- if we could comment that, you know, there's widespread exposure and there's these -- I think what I heard from both of you was neurodevelopmental, potential concerns, and that if you were going -- if OEHHA was going to prioritize it, it would be behind benzophenone-3 in terms of looking at that category of consumer products

CHAIRPERSON LUDERER: Sunscreen can -- yeah. Dr. Auyeung-Kim, did you have something else to add to that, or -- I thought you were -- it looked like you were raising your hand.

COMMITTEE MEMBER AUYEUNG-KIM: (Shakes head.)

CHAIRPERSON LUDERER: No. Okay.

All right. Any -- any other discussion?

All right. All right. Then let's proceed with the vote. So please raise your hand for high priority, putting this in the category of high priority.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Woodruff and Dr. Luderer. All right. So we have two.

And then moderate priority.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Auyeung-Kim, Dr. Carmichael, Dr. Baskin, Dr. Plopper, Dr. Allard, Dr. Hertz-Picciotto, Dr. Pessah, and Dr. Breton. All right. So that is everyone, I believe. Did I miss anyone?

No. Okay. All right.

VINPOCETINE

COMMITTEE DISCUSSON

CHAIRPERSON LUDERER: Then our next chemical is vinpocetine. And the lead discussants for this chemical are Dr. Auyeung-Kim and I.

Dr. Auyeung-Kim, do you want to begin?

COMMITTEE MEMBER AUYEUNG-KIM: Sure. I can do that. So vinpocetine is the only chemical under discussion today that does not have widespread use. It is used as a dietary supplement. Although in 2016, FDA tentatively concluded that it does not meet the definition of a dietary ingredient and is excluded from definition of a dietary supplement in the federal Food and Drug Cosmetic Act.

The FDA has already issued a warning in June of 2019 specifically about the concern about the usage of

vinpocetine in women of child-bearing potential. A rat rate -- a rat -- an animal study was conducted in rats and it was a definitive. In addition to, there was a rat embryo fetal study which has sufficient number of animals and dose range -- relevant dose route oral -- which was oral, and it was conducted under good laboratory practices.

The NTP concluded in their report published in June of 2020 that under conditions of the -- of the rat prenatal study, there was clear evidence of developmental toxicity of vinpocetine in rats attributable to the increase post-implantation loss, and increased incidences of ventricular septal defects, thoracolumbar ribs, and incomplete ossification of the thoracic center in the absence of overt maternal toxic -- toxicity.

Additionally, similar effects were also observed in a dose ranging finding studies in the rabbits with exposure.

I -- for this compound, I would say that due to the limited exposure, because it's in a specific population, and there's an active regulation by the FDA, I recommend no priority for this compound.

CHAIRPERSON LUDERER: Thank you, Dr. Auyeung-Kim.

Yes, I agree that this -- so the study -- there was really of -- only one study, but it was a very well

done study by the National Toxicology Program, as Dr. Auyeung-Kim stated. And this is -- there are no -- and there are no epidemiological studies. So I agree that there is -- there is strong evidence for developmental toxicity from this -- this study. I would -- and I also agree that the potential for exposure is not as high as many of the other chemicals that we've discussed today. It is sold as a dietary supplement.

And, you know, so I think it's probably fairly difficult to know how many people are exposed to this, continue to be exposed to this despite the FDA warning. And so I think because of that, I would put it on the moderated list, because there was -- there was a note that, at least in the NTP report, that -- that this is also taken by pregnant women. And so that is obviously a concern, so that's why I would classify it as moderate rather than no priority.

All right. So any discussion?

Patrick.

COMMITTEE MEMBER ALLARD: Yeah, I just wanted to, I guess, reiterate that point that it is sold as a supplement. It's easy to find. You can order it online and just look it up.

CHAIRPERSON LUDERER: Yep. Yep. Yep.

(Laughter.)

COMMITTEE MEMBER ALLARD: It's been sold as a life-extending chemical.

CHAIRPERSON LUDERER: Yes.

COMMITTEE MEMBER ALLARD: And I definitely flagged this when I reviewed the chemicals, because as several studies, one after the other, well conducted, even at the lowest doses tested, which, you know, was not necessarily in the --

CHAIRPERSON LUDERER: Right.

COMMITTEE MEMBER ALLARD: -- ultra low range, but still in the low range did pick up the fetal loss and post implantation loss. And that -- I mean, that is the definition of a reproductive toxicant.

CHAIRPERSON LUDERER: Right.

COMMITTEE MEMBER ALLARD: So the fact that it's publicly available and that it just comes through so clearly as a repro toxicant --

CHAIRPERSON LUDERER: Yes.

COMMITTEE MEMBER ALLARD: --- repro and dev toxicant really made me flag this a lot higher.

CHAIRPERSON LUDERER: Yeah. Any other comments on that chemical?

PUBLIC COMMENTS

CHAIRPERSON LUDERER: All right. Then we will turn to the recommendation -- let's check, are there any

public comments on this chemical, Jessica?

MEETING MODERATOR: Let's see, I am not seeing any at this time. Let me check one more -- no, we're good.

COMMITTEE DISCUSSION AND RECOMMENDATION

CHAIRPERSON LUDERER: All right. Thank you. All right. Then we will move to the vote, assuming there's no further discussion.

So I don't see any hands for further discussion, so we'll start with the vote. So raise your hand, please, if you would put this in the high priority category?

(Hand raised.)

CHAIRPERSON LUDERER: Dr. Allard.

Moderate priority.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Woodruff, Dr. Plopper, Dr. Pessah, Dr. Luderer.

And no priority.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Auyeung-Kim, Dr. Carmichael, Dr. Baskin, and Dr. Breton.

Okay. I think that was -- I got all the votes.

Then let's move on --

DIRECTOR ZEISE: Dr. Luderer, just to recap then, we've got one high, four medium, and five no.

CHAIRPERSON LUDERER: Correct.

DIRECTOR ZEISE: Okay. Thanks. Yeah.

CHAIRPERSON LUDERER: All right. So we have -- we have the potential for taking a break here or do we want to just continue and pile through to the last one.

COMMITTEE MEMBER AUYEUNG-KIM: I say we just go for it.

CHAIRPERSON LUDERER: All right.

COMMITTEE MEMBER WOODRUFF: There's more -- we have other things on our agenda besides the remaining chemicals, is that right?

CHAIRPERSON LUDERER: Yes, we do. We have the update on the California Code of Regulations chemicals that have not been tested as required, staff updates.

COMMITTEE MEMBER BRETON: I have a question.

CHAIRPERSON LUDERER: Yes.

COMMITTEE MEMBER BRETON: And that is did we -- when we were doing the PFAS, did we actually ask for public comment? Were there any public comments for that one. I feel like we might have skipped that.

CHAIRPERSON LUDERER: Let me see. I'm not -- we didn't have any listed in the agenda. Were there any? I don't remember whether I asked for public comments or not. Did we get any public comments Jessica for the perfluorinated and polyfluorinated compounds, the PFASs?

MEETING MODERATOR: I didn't see any hands go up for that. I mean we can ask now, if you want to, but I did not see any myself.

CHAIRPERSON LUDERER: All right. And I also didn't have any in the agenda that had requested it ahead of time, but thank you for noting that, Dr. Breton.

All right. Well, since we do have other business after the zearalenone, do we want to -- maybe we should take a break for 10 minutes. All right, 10 minute break. So it's 6 -- it's 4:15, so 4:25 we'll reconvene.

(Off record: 4:15 p.m.)

(Thereupon a recess was taken.)

(On record: 4:25 p.m.)

ZEARALENONE

COMMITTEE DISCUSSON

CHAIRPERSON LUDERER: All right. We can go ahead and resume then. On to our last chemical, zearalenone. That's how I want to pronounce. And the lead discussants for this chemical are Diana Auyeung-Kim and Charles Plopper.

Dr. Auyeung-Kim, do you want to start?

COMMITTEE MEMBER AUYEUNG-KIM: Sure, why not.

So zearalenone -- can I just call it ZEA -- is a naturally occurring mycotoxin with widespread exposure and has estrogenic properties. The FDA regulates mycotoxins

under the Animal Feed Contaminants Program as well as under the Food Safety Modernization Act. The FDA has not established a tolerance or developed guidance for ZEA, but has stated on the Animal Feed Contaminants Ram website, when animals or humans are exposed to ZEA at low levels, there may not be any visible symptoms as it has low toxicity. However, when ZEA is present in food at high levels or when there is consistent exposure at low levels, there have been reports of reproductive disorders and estrogenic effects.

This is noted in the numerous articles cited in the OEHHA notes and in which there were animal studies connected in mouse, rat, and pig to demonstrate the male and female reproductive effects. Animal studies were conducted -- let's see. Let's see. The developmental effects observed in both the mouse and rat studies appear to be related to maternal toxicity of decreased feed intake and/or body weight gain -- decreased body weight gain and were related to the estrogenic effects of ZEA.

In the Althali paper, pregnant mice were treated orally with 25 mg per kg ZEA and had maternal toxicity consisting of decreased weight gain and fetal effects due to the estrogenic effects. These included decreased litter weight, fetal malformations, increased number of abortions and resorbed fetuses. However, the study was

not adequately designed as it only looked at one dose level and used a small number of animals.

The other study, Kunishige and Li et al., demonstrated that ZEA effects the maintenance of pregnancy and effected the placental development in mice -- similar in mice. And similar results were observed in the rats in the Gao paper and pig in the Zhang paper. Although the pig studies, there is question on whether the ZEA -- the feed that was given also had other mycotoxins.

The epidemi studies cited by Bandera et al. and Rivera-Núñez et al. indicated that girls with detectable ZEA levels in urine were shorter and had delayed breast development. The two cited studies utilized the same cohort of girls and urine sample in their analysis.

There was -- so that resulted in some limitations, because it was conducted on a small population of girls, which is less than 200 based on a single urine sample and generally the population was homogeneous.

So ZEA has the potential for male and re -- for male and female reproductive effects. Exposure is limited by environmental conditions, because it's -- the mycotoxin is formed dependent on the humidity and temperature. And so based on discussions that we've had today, I recommend ZEA be considered for medium priority.

CHAIRPERSON LUDERER: Thank you very much.

And, Dr. Plopper, would you like to give us your thoughts on zearalenone?

COMMITTEE MEMBER PLOPPER: Sure. I think Dr. Kim did a nice job of covering most of the issues. The postnatal exposure has negative effects on female reproduction. And consistently, we're talking about 23 studies here of postnatal exposure, six of them in females and they all showed the same negative effects on ovarian and reproductive function in females. The eight male reproductive studies all found -- five of them found negative effects on sperm or spermatozoa and three of them looked at testes and found increased testis pathology.

She's already summarized the endocrine effects, which are -- tend to be negative in certain terms of female hormones like LH, and estradiol, FSH. And negative in males related to testosterone.

So I would -- I think the challenge here is that this is found in large amounts of food stuffs. And how we would go about addressing that, I don't know, but I would agree with her that it's probably a middle priority.

CHAIRPERSON LUDERER: Thank you, Dr. Plopper.

Do we have discussion from the Committee?

Dr. Pessah.

COMMITTEE MEMBER PESSAH: I was just wondering,

is there a surveillance for ZEA or are there sort of levels of where warnings are posted?

CHAIRPERSON LUDERER: As is done with the aflatoxin, for example.

COMMITTEE MEMBER PESSAH: (Nods head.)

CHAIRPERSON LUDERER: Does anybody know in the -- anyone -- staff people know about that possibly?

No.

DR. SANDY: This is Martha Sandy. I don't know. We can look into that, if you'd like, but we were not -- you mean, in food stuffs?

COMMITTEE MEMBER AUYEUNG-KIM: So in the Animal Feed Contaminants Program, there is no tolerance -- or they have not estab -- developed guidelines for ZEA, but they have for aflatoxin and one other compound.

COMMITTEE MEMBER PESSAH: What I found striking about this particular toxin, I read up a little bit on it, it's affinity for the estrogen receptor is -- it rivals that of estradiol.

CHAIRPERSON LUDERER: Yeah.

COMMITTEE MEMBER PESSAH: And it hits all of the estrogen receptors, including the GPER the cell surface receptor, which of all the compounds that we've talked about, it's -- yeah, it's a concern.

CHAIRPERSON LUDERER: Dr. Allard.

COMMITTEE MEMBER ALLARD: Yeah. I just want to add to that, if you -- if you plug this chemical into the ToxCast dashboard, you'll see that it lights up the estrogen receptor assays at extremely, extremely low level -- in the very, very low nanomolar, if not even below levels. One of the assays, one of the estrogen receptor assays that they, they even put zero, because it's -- it's beyond what they could actually put on the screen. So, yeah, it's one of the most estrogenic compounds that we had to review so far, for sure.

CHAIRPERSON LUDERER: Yeah. And I think the other thing that's notable is that for the male and female repro effects with the postnatal exposure, there were similar findings in three different species.

COMMITTEE MEMBER PESSAH: Yes.

CHAIRPERSON LUDERER: All right. Any -- any other comment?

Dr. Hertz-Picciotto.

You're muted I think again.

COMMITTEE MEMBER HERTZ-PICCIOTTO: Okay. Sorry. Yeah. I was just going to -- as a note, in 2011, I was on a national academy committee on breast cancer and the environment. And that was the first time I heard about zearalenone. And, you know, it was -- it was -- this estrogenic activity, this was brought to attention of the

committee and noted as a concern. Of course, there -- then there was even less data than there is now, but it certainly seems like a compound of concern and -- yeah, probably both for cancer and for -- and for other reproductive -- reproductive outcomes. It also -- seeing that it's used in breast enlargement supplements, it is pretty

COMMITTEE MEMBER PLOPPER: Yes.

COMMITTEE MEMBER HERTZ-PICCIOTTO: -- concerning. And I don't know if FDA has been -- has taken this up at all. But, you know, that plus it being pretty common in food stuffs. It kind of seems like it's an aflatoxin. It's kind of this -- a very similar problem, because it occurs so -- you know, it's a mycotoxin before control was considerable, I'm sure.

CHAIRPERSON LUDERER: Okay. Any additional comments?

PUBLIC COMMENTS

CHAIRPERSON LUDERER: I believe we have one public comment from Tom[SIC] Johnson of the California Rice Growers Commission. Jessica, do you have -- can you unmute, Dr. Johnson? Is he available?

MEETING MODERATOR: Let's see. Go ahead and give me that name one -- or last name one more time.

CHAIRPERSON LUDERER: Johnson.

MEETING MODERATOR: Johnson, let's see. Tim Johnson. Okay. I am going to go ahead and unmute you on my end. You can go ahead and unmute yourself and you should be good to go.

MR. JOHNSON: Thank you. Can everybody hear me all right?

CHAIRPERSON LUDERER: Yes.

MR. JOHNSON: Well, thank you. I am Tim Johnson. I'm President and CEO of the California Rice Commission. And we represent the state's rice farmers and rice millers. And so I'm going to give you a little bit of a different perspective today, really from an agricultural production perspective, maybe different than some of the comments you've heard from some of the PhDs today.

I'm going to pull out a couple of items that I think the Committee might be interested in in my comments, and I'll keep them short.

Yeah, there were a number of references the infant and toddler food survey that was done where rice was noted as having detections of ZEA. I'd look back at those studies and would just note a couple of items. In the 2007 study, zinedine -- he noted that the presence of ZEA was not found in rice in North America, but was found in rice in India, Korea, and Qatar. Most of the detections in the U.S. were noted on corn and wheat. And

those crops for food uses are primarily grown outside the stated of California, in some cases internationally.

In the 2018 Zhang study, a couple of items that I would note. They did rice and infant toddler cereal samples. Very low detection of ZEA in any of the rice-based products. Of course, we don't know where the rice was sourced from, but they did know. And maybe this would be helpful to staff that none of the detections in the study of rice or other products would be other grain-based infant and toddler cereals were detected at levels higher than the FDA action levels. So that indicated to me that FDA has spoken to this, at least with regard to agriculture of levels above which they would expect us to take action.

For the benefit of the Committee and staff at OEHHA, other published research notes that the conditions that favor the production of ZEA, that mycotoxin, are temperate climate and high grain moisture during storage. So as I looked at this and overlaid both the California and the U.S. rice industry, I was not surprised to find a very low level of findings of ZEA related to rice.

There were no reported presences of fusarium, which is the pest in the plant, that then causes ZEA under those storage conditions. In California, I was able to find, when I contacted our extension and University of

California experts, folks in the mid-south, so that would be Arkansas, Texas, Missouri, Louisiana had only indicated an incidental case of fusarium diseases in rice, and really none that were of commercial importance.

And of probably the greatest import to the Committee and the staff is the fact that rice is a grain that is harvested at high moisture certainly, but we dry that under very controlled conditions down to a very low moisture level, about 13 percent moisture, and we condition and maintain that storage and the conditions of that rice throughout the storage term, until that rice is processed. So just to gave you an idea of how the grain handling works with regard to rice.

I would just finally note that ZEA, of course, would fall into the category, we believe, of naturally occurring under Prop 65, and was noted earlier by one of the panel members, it's going to be difficult, right, for OEHHA to engage grain growers across the United States, and internationally, and moving forward on -- on a listing and safe harbor evaluation for ZEA. It will be very difficult I believe and take very -- significant amounts of resources to engage agriculture across that band.

So thank you very much. I do appreciate your opportunity to address the Committee especially at the very late hour that we have in front of you.

Thank you very much

CHAIRPERSON LUDERER: Thank you very much.

COMMITTEE DISCUSSION AND RECOMMENDATION

CHAIRPERSON LUDERER: Do we have any additional discussion by the Committee before we vote?

All right. Seeing no raised hands then, we'll proceed to the vote. So please raise you hand if you vote that zearalenone should be in the high priority category.

(Hands raised.)

CHAIRPERSON LUDERER: Okay. I see Dr. Pessah, Dr. Allard, Dr. Luderer. All right. Three votes.

And then the moderate category?

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Auyeung-Kim, Dr. Carmichael, Dr. Plopper, Dr. Hertz-Picciotto, Dr. Woodruff, Dr. Breton, and Dr. Baskin.

All right. That is everyone.

So we have completed discussion of the 22 chemicals and groups of chemicals that were on the agenda for today. So we only have a few more items on the agenda.

UPDATE OF THE CALIFORNIA CODE OF REGULATIONS TITLE 27 SECTION 27000 LIST OF CHEMICALS WHICH HAVE NOT BEEN ADEQUATELY TESTED As REQUIRED

CHAIRPERSON LUDERER: The next item is an update

of the California Code of Regulations, Title 27, Section 27000 list of chemicals which have not been adequately tested as required. So this is a ministerial item and the Committee is being asked to affirm changes in response to submissions from the Department of Pesticide Regulation and U.S. EPA. And then I will now turn to Julian for the staff presentation.

MR. LEICHTY: Okay. Thank you. So this is a consent item for the Committee. We've provided you with a staff report and recommendations for your review on November 23rd. The report summarizes information received from other relevant entities. The section 27000 list is a list of chemicals that under State or federal law require additional testing for cancer or reproductive toxicity endpoints. It's not the same list as the more well known Proposition 65 list.

So for this list, we rely on U.S. EPA and the Department of Pesticide Regulation within CalEPA to give us information about mandatory chemical testing, and -- okay. I guess we don't have the slide up, but if we did have the slide up, you would see that a chemical to be removed from the list identified by the Department of Pesticide Regulation is sodium fluoride.

MEETING MODERATOR: Yeah, apologies. I'm looking for the slide. I thought I had downloaded them. But let

me -- let me find them real quick. My apologies. Can you tell me what they're labeled under or what's the name of the PowerPoint?

MR. LEICHTY: Yeah, It's labeled Section 27000. It was in with the group of slides that I first sent.

MEETING MODERATOR: Okay. So I see a draft for that, but it's only one slide. Is that the correct one?

MR. LEICHTY: Yeah, that's -- it's -- that's the slide. It's the final slide.

MEETING MODERATOR: Okay. Okay. I got it. I'll show it right now.

(Thereupon a slide presentation.)

MEETING MODERATOR: Okay. It should be showing now.

MR. LEICHTY: So unless you have any questions, I'll turn it back to Dr. Luderer for the question and vote.

CHAIRPERSON LUDERER: All right. Do we have any questions from the panel regarding this vote on sodium fluoride?

All right. If not, then I will ask for a vote. So to vote yes to affirm the changes, raise your hands, please, if you vote yes to affirm these changes.

(Hands raised.)

CHAIRPERSON LUDERER: Dr. Pessah, Auyeung-Kim,

Allard, Carmichael, Plopper, Hertz-Picciotto, Breton, Baskin, Woodruff and, Luderer all voted yes.

All right. Thank you. Do I need to read the vote question again, since I didn't ask it in specific verbiage that I was supposed to?

CHIEF COUNSEL MONAHAN CUMMINGS: No, I don't think so. This is Carol.

CHAIRPERSON LUDERER: Okay. Thank you. All right.

CHIEF COUNSEL MONAHAN CUMMINGS: Thanks.

STAFF UPDATES

CHAIRPERSON LUDERER: All right. So the final -- the next item is staff updates. So again, I'd like to ask Julian Leichty as well as Carol Monahan Cummings to give staff updates on Proposition 65 listings, regulations, and litigation that have taken place since our last meeting.

(Thereupon a slide presentation.)

MR. LEICHTY: Okay. So since the Committee's last meeting, one safe harbor level has been adopted in regulation for a reproductive toxicant, a maximum allowable dose level of 7.2 micrograms per day for the dermal route of exposure and 0.58 micrograms per day for oral inhalation was adopted for chlorpyrifos effective October 1st, 2020. And now I'll turn it over to Carol.

CHIEF COUNSEL MONAHAN CUMMINGS: Okay. So I

have -- can you put the next slide up. Hopefully, it's mine.

NEXT SLIDE

CHIEF COUNSEL MONAHAN CUMMINGS: Okay. So our office does other regulatory work besides the safe harbor levels, which you guys peer review the safe harbor levels, so we want to make sure you know when we adopt them.

Oop, my slide went away.

So we have other regulatory actions that we take. And in the last couple of years we've been primarily working on changes to the warning regulations.

Are you going to be able to get the slide back up? I don't have a copy of that one.

MEETING MODERATOR: Yeah. Sorry about that. Someone took the control away from me. I'm bringing it back.

CHIEF COUNSEL MONAHAN CUMMINGS: Okay. So two of these regulations that -- that -- one the responsibility to provide warnings was already adopted effective April 1st, 2020. That one just gave some additional information to businesses on who in the chain of commerce needs to provide warnings. And basically, it -- you know, it starts at the manufacturer and goes all the way down to the retailer. And so that regulation kind of clarifies that for them.

We also have proposed a regulation that would amend the current warnings for alcoholic beverages and add some additional methods for providing those warnings. We didn't change the text of the warnings, just the ways that it can be given, primarily to adopt some more recent changes in the way the industry sells things, like online or through apps. And we basically adopted a -- the provisions of a settlement that the Attorney General's Office had with a number of alcoholic beverage retailers. That one is almost final. We're waiting for a final approval from the Office of Administrative Law, which we expect, I believe, in January.

So in terms of -- sorry. Sorry. The last one -- excuse me, just a sec.

Okay. The last one has to do with chemicals that are created by cooking or heat processing. And that's a brand new regulation. We haven't had one like that before. It's currently focused on acrylamide in foods, which is listed as both a reproductive toxicant as well as a carcinogen. And we are establishing concentration levels for food products or food categories that businesses can use to determine whether they need to have a warning for those exposures. That regulation is still in process and we're reviewing the first round of comments we received on it.

Next slide.

NEXT SLIDE

CHIEF COUNSEL MONAHAN CUMMINGS: All right. I wanted to just give you a quick update on the litigation that we have been involved in. And we've actually had a pretty good year in terms of outcomes for litigation. The chemical glyphosate, which you talked about today, has been listed as a carcinogen for some time. And there's a case pending now in the Ninth Circuit where some industry groups have challenged the warnings for glyphosate based on the first amendment. In that case, the Attorney General actually is the defendant in that case now. And the court has -- the trial court has ruled that the warnings are unconstitutional under the first amendment and so we're at the court of appeal to see if that ruling is going to stand.

For some of the State court proceedings, there's -- many years ago, your Committee considered the listing of BPA as a reproductive toxicant and didn't list the chemical. Subsequently, OEHHA did through a different mechanism based on a report from NTP. We were immediately sued regarding that listing and it's been -- that was like in 2013, I believe. And it's been winding its way through the court system. Very recently, the court of appeal upheld the trial court finding that it was a valid listing

of the chemical.

Since those -- that time has passed, we've also listed it as a female reproductive toxicant I think by this Committee. So it is now -- now will be listed as both a developmental and female reproductive toxicant.

The case regarding DINP which is another phthalate, was upheld by the court of appeal. That's a cancer listing, but it was the first challenge we've had go all the way to the court of appeal on a Committee listing. And it was interesting for two reasons. One was that the -- one of the bases for challenging the listing was the -- that the Chair of the Committee, the CIC, made some remarks towards the end of the meeting about considering animal data. And the argument was that that changed the mind of all of the members of the Committee. Another argument was that there was insufficient scientific data to show that DINP, in fact, causes cancer.

The trial court, court of appeal upheld the listing, and the Supreme Court -- State Supreme Court declined to review it, so that case is now final, the chemical is on the list.

We've get a couple of cases that have to do with coffee. And the -- coffee is -- contains acrylamide, but it contains a lot of other things. And our office fairly recently adopted a regulation finding that coffee doesn't

require warnings under Prop 65. It's a very unusual thing for us to do, but we did it based on the evidence that we had available for coffee, not acrylamide in particular. And there's been some litigation against both our office, as well as the -- a number of coffee makers and sellers.

So far, the court has entered judgment against the Center for Education -- or Council for Education and Research on Toxics as to OEHHA. And we expect that -- that case to go up on appeal, but -- and then in the Starbucks case, the court has found that our regulation, in fact, is valid and basically dismissed the case against the coffee makers and sellers.

The last item is a current relatively new case that is challenging OEHHA's decision not to list processed meats, based on a finding by IARC that some processed meats can cause cancer. We declined to list and the PCRM has sued our office to -- to challenge that decision. There's a hearing in February. The first hearing is in February on this case.

So does anybody have questions on any of those?

CHAIRPERSON LUDERER: Dr. Woodruff.

COMMITTEE MEMBER WOODRUFF: Yeah. I was curious about the processed meat. So I thought that anything that was listed by an authoritative body automatically goes on the list. But is that not true, OEHHA has some

discretion? Is that why you guys didn't list it?

CHIEF COUNSEL MONAHAN CUMMINGS: Well, for this one, this is a -- would be a listing under the Labor Code provision of Prop 65. And that is a ministerial listing. However, our office has to be able to determine what the thing is that's being listed.

COMMITTEE MEMBER WOODRUFF: Oh.

CHIEF COUNSEL MONAHAN CUMMINGS: And based on the IARC document, we weren't really able to establish what would be listed and what wouldn't be listed under -- using that document, so we declined to list it, at least at this time.

For other authoritative bodies though, we go through a regular -- much like a regulatory process with public input and a number of steps before we determine whether or not a chemical should be listed, we compare the information that's available from the authoritative body to our regulation, and the criteria there, and determine whether it should be listed. So we do have a little discretion there, but mostly it's just to determine whether or not the chemical meets our criteria.

COMMITTEE MEMBER WOODRUFF: All right. Thank you. That was interesting.

CHAIRPERSON LUDERER: All right. Then if we don't have any additional questions or discussion on that

topic, thank you very much both of you for those updates.

And finally, I'd like to ask Dr. Zeise to summarize the Committee actions.

SUMMARY OF COMMITTEE ACTIONS

DIRECTOR ZEISE: Okay. Thank you. So the Committee did a lot of work today. And I'll summarize all the recommendations of the Committee.

So the Committee prioritized -- gave us recommendations for priorities for 22 chemicals. And seven of them fall into what I'd say a majority of votes saying high. And so I'll just go through them in the order of strength of priority.

So there were four where there was a unanimous vote that they should be high. That was benzophenone-3, bisphenol S, PFDA, and PFNA. And then there was a vote of nine high to one medium for diazinon and glyphosate. And then for PFHxS, there was a seven high to three medium -- and three medium, so those are all in the majority high category.

And then there were various split votes. I'll talk about the mediums going from what would be considered maybe a medium/high to a medium/no. So imidacloprid there was a split of five high, five medium. Zearalenone, there was three high, seven medium. Domoic acid, I guess that should have been more at the top, because that was -- no,

this is the right place, one high and nine mediums. Titanium dioxide two high, eight mediums. I should have rotated with that one. Manganese and PFUnDA unanimous on medium. Butyl benzyl phthalate[SIC], one high, eight medium, one no. Acetamiprid, nine medium, one no. Clothianidin, seven medium, three no. Methylparaben, six medium, four no. So that's the set of ten mediums.

Yes, Dr. Hertz-Picciotto.

COMMITTEE MEMBER HERTZ-PICCIOTTO: Yeah, what did you say PFNA was? I didn't hear it.

DIRECTOR ZEISE: Unanimous -- unanimous high.

COMMITTEE MEMBER HERTZ-PICCIOTTO: Okay. And then PFDA also?

DIRECTOR ZEISE: Unanimous high.

COMMITTEE MEMBER HERTZ-PICCIOTTO: Oh, okay. I didn't hear those. Okay.

DIRECTOR ZEISE: And then vinpocetine was one high, four medium and five no. Exact split on thiamethoxam five medium, five no. And then unanimous noes on diethyl phthalate, isobutyl paraben, and propyl paraben.

So quite a list. So we really thank you for taking all the time to provide those recommendations, both time preparing for the meeting and all the hard work getting to that point. So thank you very much to the

Committee.

I also want to note that early on in the meeting, there was a comment from the Committee that we should start exploring more effective ways of grouping chemicals, when should we group them, when should we not group them. And so we'll be going back and thinking -- thinking about that issue.

And then throughout the meeting, we heard a lot of comments on -- not a lot, but some comments on the document and how we presented information. And I just want to acknowledge that we took in those comments and we'll be integrating them into the way in which we do business next time. So thank you for those.

So I want to just step back now a thank the facilitator Jessica Raines of LogMeIn for facilitating the meeting. I want to thank the commenters and the audience for participation and for your comments that were very, very helpful I'm sure to the Committee in reaching their decisions. And then thank you, of course, the RCHAB staff and to the OEHHA staff for all the hard work in putting the materials together, to Implementation and Legal for all their support work for this meeting, and then once again just to close with a huge thank you to the Committee for hanging in there for all your hard work, and your time, and just wishing you very safe and happy Holidays.

And again really appreciate all the careful thinking.

So with that, I'm going to turn it back over to Ulrike to -- to Dr. Luderer to adjourn the meeting.

CHAIRPERSON LUDERER: Thank you, Dr. Zeise. I also want to thank all the staff for putting together this document, which was -- really represented a lot of work and was excellently done, so -- and wish everyone a safe and healthy holiday season.

And I now adjourn the meeting. Bye-bye everybody.

(Bye-byes.)

(Thereupon the Developmental and Reproductive Toxicant Identification Committee adjourned at 5:00 p.m.)

CERTIFICATE OF REPORTER

I, JAMES F. PETERS, 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, Developmental and Reproductive Toxicant Identification Committee was reported in shorthand by me, James F. Peters, a Certified Shorthand Reporter of the State of California, and thereafter transcribed under my direction, by computer-assisted transcription.

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

IN WITNESS WHEREOF, I have hereunto set my hand this 12th day of January, 2021.

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