VIDEOCONFERENCE MEETING

STATE OF CALIFORNIA

ENVIRONMENTAL PROTECTION AGENCY

AIR RESOURCES BOARD

SCIENTIFIC REVIEW PANEL

ON TOXIC AIR CONTAMINANTS

ZOOM PLATFORM

FRIDAY, OCTOBER 15, 2021

9:31 A.M.

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

APPEARANCES

PANEL MEMBERS:

Cort Anastasio, Ph.D., Chairperson

Ahmad Besaratinia, Ph.D.

Paul D. Blanc, M.D.

S. Katharine Hammond, Ph.D.

Michael T. Kleinman, Ph.D.

Joseph R. Landolph, Jr., Ph.D.

Karen Messer, Ph.D.

Lisa A. Miller, Ph.D.

Beate R. Ritz, M.D., Ph.D., M.P.H.

REPRESENTING THE AIR RESOURCES BOARD:

Patrick Gaffney, Staff Air Pollution Specialist, Criteria Pollutant and Air Toxics Reporting Section, Greenhouse Gas and Toxics Emission Inventory Branch, Air Quality Planning and Science Division

Anne Klein, Air Pollution Specialist, Toxics Inventory and Special Projects Section, Air Quality Planning & Science Division

Lori Miyasato, Ph.D., Panel Liaison

Gabe Ruiz, Manager, Toxics Inventory & Special Projects, Air Quality Planning & Science Division

REPRESENTING THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT:

John Budroe, Ph.D., Chief, Air Toxicology and Risk Assessment Section

Daryn Dodge, Ph.D., Air Toxicology and Risk Assessment Section

INDEX

INDEX CONTINUED

PROCEEDINGS

CHAIRPERSON ANASTASIO: Good morning and welcome to the October 15th, 2021 meeting of the Scientific Review Panel. I'd like to welcome everybody to the webcast. I'd like to thank the Panel members for attending today. I want to remind everyone that this will be recorded and is being recorded. We're going to start with Panel introductions.

Before we do that, I'm happy to say that Paul Blanc has been reappointed as the Senate Rules appointee in occupational medicine and Mike Kleinman and Beate Ritz's reappointments were announced earlier this year. So thank you for joining us for another term, Paul. We appreciate it.

I'm just going to call out Panel members in order on my screen. Please just briefly introduce yourself.

Mike.

PANEL MEMBER KLEINMAN: Good morning. I'm Mike Kleinman. I'm a professor in the Department of Occupational and Environmental Health in UC Irvine and I'm the co-director of the Air Pollution Health Effects Laboratory.

CHAIRPERSON ANASTASIO: Great. Thank you, Mike.

Joe.

PANEL MEMBER LANDOLPH: I'm Joe Landolph, Jr. I

have a PhD. I'm associate professor of molecular and microbiology, and pathology, and immunology, and a member of the USC Norris Comprehensive Cancer Center at the University of Southern California. And I study cell transformation and mutagenesis in mammalian cells.

CHAIRPERSON ANASTASIO: Okay. Thank you, Joe.

Karen.

PANEL MEMBER MESSER: Good morning. I'm a professor in the Division of Biostatistics at the Wertheim School of Public Health at UC San Diego in their Health Sciences. I'm the Director of Biostatistics at the UCSD Moores Cancer Center.

CHAIRPERSON ANASTASIO: Thank you, Karen.

Lisa.

PANEL MEMBER MILLER: Good morning. I'm Lisa Miller. I'm a professor in the School of Veterinary Medicine. And I serve as the Associate Director of Research at the California National Primate Research Center. And my expertise is in respiratory immunology, primarily in large animal models.

CHAIRPERSON ANASTASIO: Thank you, Lisa.

Ahmad.

Sorry, Ahmad?

PANEL MEMBER BESARATINIA: I'm sorry. Good morning. This is Ahmad. I'm a professor of preventive

medicine at Keck School of Medicine of USC here in Los Angeles. I'm a cancer biologist by training and my research areas are on environmental carcinogenesis.

CHAIRPERSON ANASTASIO: Great. Thank you, Ahmad. Beate.

PANEL MEMBER RITZ: I'm Beate Ritz. I'm a MD, PhD, epidemiologist. I'm also co-appointed in environmental health and in neurology at the UCLA Schools of Public Health and of Medicine. And my research focuses on environmental epidemiology, mostly pesticide and air pollution exposures in just about every outcome.

CHAIRPERSON ANASTASIO: Okay. Thank you, Beate. Kathy.

PANEL MEMBER HAMMOND: Good morning. I am a professor of environmental health sciences at the School of Public Health at Berkeley. And my research area focuses on exposure assessment for both occupational and environmental epidemiology sets.

PANEL MEMBER BLANC: Kathy, there's something not right with your sound. I don't know if it's the ear phones or what it is.

PANEL MEMBER HAMMOND: Got it. Do you want me to repeat that, Cort?

CHAIRPERSON ANASTASIO: No, I think we're good. We could catch it, but thank you, Paul. Yeah, you're much

clearer now.

PANEL MEMBER HAMMOND: Good.

CHAIRPERSON ANASTASIO: Okay. And our newest member, Paul Blanc.

PANEL MEMBER BLANC: Oh, yeah. This all reminds me, you know, once I was introduced to Dolly Parton. And I was introduced as an expert in environmental causes of cancer. And Dolly looked at me and she said, "Oh, my. Doesn't that sound impressive"?

Well, I'm very impressed by everybody's expertise. And I'm just a poor country lawyer, but I also am at the University of California, San Francisco in occupational and environmental medicine and also am trained in medical toxicology.

CHAIRPERSON ANASTASIO: Great. Thank you, Paul.

And I'm Cort Anastasio. I'm Chair of the Panel and I'm a professor in the Department of Land, Air, and Water Resources at UC Davis, and I'm an atmospheric chemist.

So to move on to the meeting. We have two major items today. The first will be from OEHHA. It's 1-bromopropane cancer inhalation unit risk factor. And the second major item is from CARB. It's the AB 2588 air toxic hot spots emissions inventory criteria and guidelines regulation.

The AB 2588 presentation is going to be in two parts. The first part will be a retrospective discussing what CARB has done over the past few years related to updating Appendix A of the EICG. And then the second part will be a prospective looking forward to next rounds of additions of chemicals to Appendix A.

So we are going to accept verbal and written through the chat public comments only on part two, only on the prospective part. So if people want to comment on that, they can later.

All right. So we're going to start off with a bang, the 1-bromopropane Cancer inhalation risk -- unit risk factor document. Before we get into the details of that, I want to introduce the new Chief of the Air and Site Assessment and Climate Indicators Branch at OEHHA, Dr. Kannan Krishnan. His branch oversees the development of these health risk assessments under the air toxic hot spots program, such as the 1-bromopropane IUR we'll be discussing today.

So Dr. Krishnan, would you like to say a few words?

DR. KRISHNAN: Thank you. Good morning, everyone. Welcome to the session today. I am Kannan Krishnan, as mentioned previously, and the Chief of Air and Site Assessment and Climate Indicators Branch at OEHHA

since July of this year.

Prior to coming to OEHHA, I was a professor and Chair of the Department of Occupational and Environmental Health at the University of Montreal, Canada, where I was also Associate Dean of Research at the School of Public Health.

Most recently, I was the Chief Scientific Officer of the Quebec Occupational Health and Safety Research Institute. I'm a toxicologist by training and recognized for contributions in the area of physiologically based pharmacokinetic modeling - it's called PBPK modeling - and its applications in risk assessment, a variety of like high dose to low dose, route to route, interindividual, as well as population variability of a number of chemicals, as well as we work on structure property relationship modeling and mixtures toxicology.

Wonderful being here and I look forward to the proceedings today. Thank you.

CHAIRPERSON ANASTASIO: Great. Thank you, Dr. Krishnan. Welcome to California and welcome to California EPA.

Okay. So we're going to go start with a 1-bromopropane cancer inhalation unit risk factor. This document from the Office of Environmental Health Hazard Assessment was released for public review and comment on

May 7th, 2021. The document was revised and the Scientific Review Panel, or SRP, draft, which is dated September 2021, was sent to the full Panel for review and was also posted on OEHHA's webpage for the public.

Today, we're going to start with a presentation from OEHHA staff on the proposed cancer inhalation unit risk factor for 1-bromopropane. And then we'll have a discussion of the Panel and we'll give our feedback to OEHHA staff on this IUR. So to start, I'm going to introduce Dr. Don -- John Budroe who's chief of OEHHA's Air Toxicology and Risk Assessment Section.

John.

DR. BUDROE: Good morning. And thank you, Dr. Anastasio. And in turn, I would like to introduce Dr. Daryn Dodge. He's the lead on the 1-bromopropane cancer inhalation unit risk factor document and he'll be making presentation on the document.

Unfortunately, his webcam is not working this morning, but his audio is. So although you won't be able to see him, you will be able to hear him and the slides will be presented.

Dr. Dodge.

DR. DODGE: Thank you, Dr. Budroe.

Are the slides going to be coming up here in a moment?

(Thereupon a slide presentation.)

DR. DODGE: Okay. I'll get started.

Okay. I'll begin by talking about -- a little bit about the chemical itself and why we chose to derive and inhalation unit risk factor for 1-bromopropane. And then we'll go -- or I'll go step by step on how we derived the cancer inhalation unit risk factor.

Okay. Next slide.

--o0o--

DR. DODGE: 1-bromorpropane is also referred to as n-propyl bromide, although in most publications you'll see it named as 1-bromopropane. It's a colorless liquid at room temperature, but with aging it turns yellow-ish. It's soluble in organic solvents and slightly soluble in water, 2,450 milligrams per liter of water. It has a boiling point of 71 degrees Celsius. And the vapor pressure is 110.8 millimeters mercury, so it's considered a volatile organic chemical.

Okay. Next slide.

--o0o--

DR. DODGE: 1-bromopropane is currently listed as a carcinogen under the California Proposition 65 Program. It is also listed by the International Agency for Research on Cancer, or IARC, as a Group 2B carcinogen, or otherwise possibly carcinogenic to humans.

Its uses primarily is as a solvent vehicle for adhesives in laminates and foam products, and as degreasing or cleaning agent for metals, plastics, optics and electronics.

It is promoted as an alternative to ozone depleting chlorofluorocarbons. And that is one of the reasons we saw increased use of this occupationally as a solvent in degreasing agents starting in the mid to late 1990s.

It is also an alternate solvent in modified perchloroethylene dry-cleaning machines in California, but currently its use in dry-cleaning facilities is quite limited. I think there might be only one or two facilities that actually use 1-bromopropane.

Okay. Next slide.

--o0o--

DR. DODGE: California emissions. We have very limited data on 1-bromopropane emissions. And I'll be referring to 1-bromopropane as 1-BP occasionally. It's currently not reportable under the Hot Spots Program, but this will -- this should change next year, hopefully, under the Hot Spots Program. Facilities will need then to quantify it and quantify its emissions.

There was a statewide California survey conducted by the California Air Resources Board in 2011. And they

reported a total of 160.7 tons of 1-BP, or 1-bromopropane, due to solvent cleaning operations.

Next slide.

--o0o--

DR. DODGE: Metabolism of inhaled 1-bromopropane in rodents is primarily through oxidative metabolism via P450 enzymes, conjugation with glutathione, and debromination. The majority of the absorbed of 1-BP maybe excreted unchanged or as CO2 in exhaled area within four hours. This particular study was in IV, or intravenous, study in rodents. But inhalation, you see the same numbers as you do with injecting into the IV. The absorbed 1-BP in exhaled hair is 41 to 71 percent in the study. And when it's exhaled as CO2, it's about 10 to 31 percent.

Radiolabeled 1-BP recovered in urine ranged from 17 to 23 percent. The main metabolite -- urinary metabolite excreted was n-acetyl-s-propylcysteine. This consisted of 37 percent of the total urinary metabolites. This metabolite is found in the urine of 1-BP workers and it is found in biomonitoring studies of children and pregnant women. Other metabolites -- minor metabolites include 1-alpha-bromohydrin in glycidol. Both are known mutagens.

Next slide.

--o0o--

DR. DODGE: NIOSH, which stands for the National Institute of Occupational Safety and Health, observed a strong association between the time-weighted average inhalation exposure of 1-BP in workers and the urinary metabolite n-acetyl-s-propylcysteine. And one of their conclusions was that this metabolite is an effective biomarker for exposure of 1-BP workers.

There were two biomonitoring studies that have come out recently. The first is the National Children's Vangard Study conducted 2009 to 2010. And they found this metabolite, n-acetyl-s-propylcysteine in 99 percent of urine samples of third trimester pregnant women. There are nearly 500 women in this study.

There was also an NHANES study conducted from 2011 to 2012. NHANES stands for the National Health and Nutrition Examination Survey, which is conducted occasionally, where mean urinary levels of n-acetyl-s-propylcysteine was 2.6 and 3.3 in boys and girls respectively. These particular levels in urine is similar to what was seen in the third trimester pregnant women of the Vangard study.

So these surveys suggest widespread non-occupational exposure to 1-BP. Although, exposure to other chemicals may result in the same urinary metabolite,

this has not been explored in these biomonitoring studies. They just suggested that there was exposure to 1-bromopropane, or 1-BP, but it's not clear at this point what other chemicals they could have been exposed to that result in the same metabolite.

Next slide.

--o0o--

DR. DODGE: Okay. I'll start with the NTP, or National Toxicology Program, study here, in which they performed a whole body inhalation cancer bioassay in rats and mice, which was concluded and published in 2011. This is the only long-term or lifetime rodent study available for 1-bromopropane.

In this study, which was two years, they used their standard species and strain of rats and mice, F344 rats, and B6C3F1 mice. There were 50 animals per exposure group, per sex, per species. In rats, the exposures were 0, 125, 250, and 500 parts per million for 6.2 hours a day, or six hours and 10 minutes per day. This was for five days a week for 105 weeks, or roughly two years.

In mice, the exposure duration was the same, six hours, 10 minutes per day, five days a week, 105 weeks. However, the high-end exposure was lower. The exposures were 0, 62.5, 125, and 250 parts per million. They did not have a 500 parts per million group for mice, because

this reached a threshold where you saw severe liver damage. In fact, if you exposed the mice to 500 parts per million or greater, many of them may die in the first week of exposure due to liver damage.

Next slide.

--o0o--

DR. DODGE: Following the two-year exposure in rats and mice, there was an increased tumor incidence in male and female rats. We'll talk about the rates here in this first slide. In male rats, you saw an increase in epithelial skin tumors or if they were of epithelial origin. This is included keratoacanthoma, basal cell adenomas, basal cell carcinoma, and squamous cell carcinoma.

These skin tumors combined resulted in a statistically significant increase in all exposure groups compared to the control group. In addition, there was a positive trend for this tumor type. In other words, as dose increased, you saw an increase incidence of these tumors. In female rats, there was an increase in large intestine adenoma in the high dose group, the 500 part per million group. In addition, there was a positive trend for this tumor type.

In male rats, the NTP also saw an increase in large intestine adenoma, but the increase where there was

only a few animals in the -- in the exposure groups that showed this particular tumor. This resulted in no difference from control and no positive trend for the tumor type. However, because these tumors are very rare in rats, the NTP considered it to be caused by 1-bromopropane.

Next slide.

--o0o--

DR. DODGE: In mice, there was increased tumor incidences in the females only. These were lung tumors, alveolar/bronchiolar adenoma and carcinoma combined. The increases were statistically significant in all exposure groups compared to the control group, and there was a positive trend for this tumor type.

In male mice, there was no increase in tumors that were suspected to be due to 1-BP exposure.

Next slide.

--o0o--

DR. DODGE: Now, this is the only long-term cancer study in animals. However, there is other supporting data. Metabolism of 1-BP produces effects similar or that other carcinogens are known for, such as oxidative stress via glutathione depletion and immunomodulation.

There are structurally related brominated

hydrocarbon compounds that also cause tumors in the same organs and tissues as 1-BP. These include 1,2-dibromoethane, tribromomethane, 1,2-dibromo-3-chloropropane, and bromodichloromethane.

1-BP metabolites form by cytochrome P450 mediated oxidation are also known to be direct acting mutagens. And I mentioned these earlier, alpha-bromohydrin and glycidol.

Next slide.

--o0o--

DR. DODGE: There have been genotoxicity studies with 1-bromopropane, although it's a relatively small genotoxicity database compared to some of the other major compounds that the NTP has examined.

Now, I'll go over these briefly. There were three studies that looked at DNA damage. This was with the comet assay. However, they were equivocal in their findings. In other words, it wasn't clear, there was a positive that the 1-BP was positive for DNA damage by these comet assays.

However, there was two DNA adduct formation studies, one in vitro and one in vivo, and these were both positive. And we're talking about N7-guanine adducts here. There was one study that looked at induction of DNA repair, and this was negative.

There are three good bacterial mutation assays available. Two were negative, however, one was positive. And the one that was positive did the best job in preventing evaporation of 1-BP during incubation of 1-BP with bacteria.

There's one study that looked at mammalian cell gene mutation. And this was with mouse lymphoma cells, and this was positive.

There were two studies that looked at chromosomal damage in vivo, and these were both negative, as well as the transgenic rodent mutation assay also negative.

Next slide.

--o0o--

DR. DODGE: So to recap, there are no epidemiology findings for carcinogenicity, although exposure data of sufficient size and duration may not exist yet, and this is because use of 1-bromopropane didn't increase dramatically until around the mid to late 1990s, at least occupational use.

One rodent lifetime inhalation study found that 1-BP is carcinogenic in multiple species and induced tumors in one or more sites in rats. There are some positive genotoxicity studies. DN adduct formation in both in vivo and in vivo -- in vitro and in vivo. Mutagenic in a closed system bacterial Ames assay, and it

induced mutations in vitro in mouse lymphoma cells.

There are -- there are also structurally related brominated compounds that produce similar tumors in lifetime rodent studies.

Combined, these factors point to a potential for 1-BP to induce tumors in humans.

Next slide.

--o0o--

DR. DODGE: So now we'll talk about the inhalation unit risk factor derivation. The first step in IUR, or inhalation unit risk factor derivation, is converting the NTP tumor incidence into what's called an effective tumor incidence. The effective tumor incidence is the number of tumor-bearing animals over the number of animals alive at time of first occurrence of the tumor. This removes animals from the assessment that die before they were considered at risk for tumor development.

Next slide.

--o0o--

DR. DODGE: In this slide, we compare the NTP tumor incidence for effective -- the NTP tumor incidence with the effective tumor incidence. The middle column labeled "NTP Incidence", you'll notice that in the denominator, there are 50 animals.

Now, in the column to the farthest right, the

"Effective Tumor Incidence", the one in bold, you'll notice that the denominator is lower, sometimes slightly lower, sometimes a little more lower. And this is because again animals were removed from the assessment that died before they were considered at risk for tumor development.

Next slide.

--o0o--

DR. DODGE: In male rats, survival was significantly reduced at 500 parts per million. The life table pairwise comparison P value was 0.033. There was also decreased survival greater than 15 percent compared to controls by week 85 of the study. And most of these early deaths were due to treatment-related chronic inflammation. Now, in a situation like this, we didn't use -- we couldn't use the normal modeling that we'd use, so we'll discuss this in a few slides.

Next slide.

--o0o--

DR. DODGE: To determine cancer potency, we also need to convert the 1-BP air concentration to an average daily dose, expressed as milligrams per kilogram body weight per day. The dose is -- the equation is shown here. The dose is equal to the inhalation rate, or IR, times C, the concentration, divided into the body weight, where C, the concentration, is time adjusted to an annual

average. The exposures were 6.2 hours per day, and this is divided into 24 hours, and they were five days a week, this is divided into seven days. Hence, we get an annual average.

Body weight is average over the two years of exposure in the NTP study. Body weights were measured once per week in the first year of the study and then for most of the second year of the exposure, they were measured every four weeks.

The inhalation rate is an equation based on the body weight of the animals. And this is at the bottom of the slide for rats. It is -- this regression analysis equation was developed by OEHHA in 2018 based on up-to-date data on body weight and inhalation rate in rats.

In mice, we used the linear regression equation by Anderson and this was published in 1983. So you just simply plug in the body weight into this equation and you get the inhalation rate.

Next slide.

--o0o--

DR. DODGE: So these are our doses expressed as milligrams per kilogram body weight per day in rats and mice.

Next slide.

--o0o--

DR. DODGE: We now have the fraction affected, which is the effective tumor incidence and the dose, expressed in milligrams per kilogram body weight per day. We can now run a multi-stage cancer model in the Benchmark Dose Software by U.S. EPA. And this was used to determine the cancer potency for female rat and female mouse tumor data.

Now, as I mentioned earlier, there was a decrease survival of male rats. I'm sorry, I probably mentioned -- I should say that it was female rats and female mice. I may have not said that right in the first bullet there.

Now, for decreased survival in male rats, we used the multi-stage Weibull model. And this is a time-to-tumor model to account for intercurrent mortality. It takes into account the day of death into the model. Potency values were derived using a benchmark dose of five percent with five percent extra risk to calculate the benchmark dose.

The 95 percent lower confidence bound on the effective dose producing a five percent response is called the BMDL05 and is used to calculate cancer potency. So the cancer slope factor is 0.05 divided into the BMDL05.

Next slide.

--o0o--

DR. DODGE: Cancer slope factors were calculated for tumors with a statistically significant tumor incidence on pairwise comparison to controls and a positive trend for dose response.

These included skin tumors of epithelial origin in male rats, large intestine adenomas in female rats, and the lung tumors in female mice. Again, we did not develop a cancer slope factor in male mice, because 1-BP did not result in increased tumors in male mice.

Next slide.

--o0o--

DR. DODGE: So we have a cancer slope factor based on the animal or rodent we now have to extrapolate to human. And this is done with the equation in the middle of the slide and is based on body-weight scaling to the three-fourth's power.

So in this equation, we have the cancer slope factor for human is equal to the cancer slope factor in the animal, times the body weight of the human, divided into the body weight of the animal, to the one-fourth power. This interspecies scaling factor accounts for pharmacokinetic differences, as well as pharmacodynamic considerations.

Next slide.

--o0o--

DR. DODGE: So here is a table of the results from the benchmark dose analysis. The first five columns, the AIC, or Akaike information criterion, the P value, the BMD, BMDL05, and the rodent cancer slope factor, those are all generated by the U.S. EPA -- the U.S. EPA modeling -- bench dose modeling.

The last column on the far right is the cancer slope factor for human, expressed as milligrams per kilogram per day to the minus one. This was calculated using the equation in the previous slide. Now, the numbers in this column are in bold. For male rat skin tumors combined, we've got a cancer slope factor of 0.0053. In female rats for large intestine tumors, it was a smaller cancer slope factor of 0.0017.

However, in female mice, the lung tumors generated the highest cancer slope factor of 0.013. Lung tumors in female mice provided the highest cancer slope factor value, establishing this tumor as the most sensitive endpoint, or 1-BP-induced carcinogenicity.

Next slide.

--o0o--

DR. DODGE: This is the Benchmark Dose Multistage Cancer Model plot fit to the alveolar/bronchiolar lung tumors in female mice exposed to 1-BP. In this graph, the X axis on the bottom is dose. The Y axis on the left side

is response or the effective tumor incidence.

As you can see there is a positive trend for this tumor type. As you go from left to right, the dose response increases. As dose increases, the incidence of this tumor increases.

In the lower left, we have a orange line -- vertical orange line and that points to the BMD for five percent response rate on the X axis or dose, and the blue line to the left -- the vertical blue line to the left, that is your BMDL05 for the 95 percent lower confidence bound.

Next slide.

--o0o--

DR. DODGE: Now, we've been talking about cancer slope factors. However, this document is called an inhalation unit risk for 1-bromopropane. So here we get to development or Calculation of the inhalation unit risk factor. The inhalation unit risk is equal to the cancer slope factor, times the breathing rate, divided into body weight, times a conversion factor. So the cancer slope factor we are using is 0.013 milligrams per kilogram body weight per day to the minus one based on the tumors found in female mice. The human breathing rate used in this equation is default of 20 cubic meters per day in humans. The average human body weight used was 70 kilograms.

The milligram to microgram conversion factor was 1,000. This resulted in a inhalation unit risk of 3.7 times ten to the minus six. And this is in units of micrograms per cubic meter to the minus one.

So what this number means is if there is lifetime exposure to one microgram per cubic meter of 1-BP, this will result in an extra cancer risk of 3.7 chances in a million.

Next slide.

--o0o--

DR. DODGE: During the public comment period, we had no public comments submitted. However, since the public comment period, we did make a few changes to the document. U.S. EPA came out with a TSCA reference on 1-bromopropane, in which they had some good comments and analysis in their report. So we included some of that in our document as well. Specifically, these are comments on n-acetyl-s-propylcysteine as a biomarker on page 15. And the -- some of the advantages and limitations of several of the 1-BP genotoxicity studies, this was on page 19.

In addition, added a few -- added a few sentences regarding N7-guanine adducts on page 17 of the genotoxicity section. And we added a summary of the BioReliance bacterial mutation study, or assay, on page 18, and removed the Elf Atochem study, which was a

bacterial mutation assay. The reason we removed the Elf Atochem study is we could not obtain the full report. All we had was a brief summary of their results. So I could not describe or assess their methodology and their results.

Next slide.

--o0o--

DR. DODGE: Well, that concludes my presentation and we can open it up to questions now.

CHAIRPERSON ANASTASIO: Great. Thank you very much, Daryn. We appreciate your presentation and your work on this carcinogen. So the leads for 1-bromopropane were Ahmad and Karen. So, Ahmad, can you get us started off?

PANEL MEMBER BESARATINIA: Sure. Thank you, Cort. Well, this is a very well written report. It's organized nicely and it's easy to follow. Data presentation is clear and discussion of the results and conclusions are fine, except for a few instances that may require some additional information or clarification.

There are also a few other areas in the document that could use some revisions. I start with the more general comment. Firstly, the up-to-dateness of this report. The time frame of coverage for this report could be spelled out preferably if the pain document.

I notice somewhere in preface, I think it was page four, it stated that the literature summarized and referenced in this document covers the relevant published report for 1-BP through spring 2021. Well, looking at the bibliographic list, I see very few recent publication. As a matter of fact, the most recent journal articles cited in this report are only a couple of studies from 2018 and 2019, nothing from 2020 or 2021.

I did a quick PubMed search and came across several pertinent studies published in 2020, as well as in early 2021. They cover various topics related to this report, including how 1-BP can cause oxidative stress induce apoptosis, and this regulates signaling pathways that are important in carcinogenesis.

Also there are newer much more comprehensive biomonitoring studies on 1-BP, both in occupationally or environmentally exposed individual, as well as in experimental mice. Inclusion of these studies would make the report more comprehensive and up to date.

Along these lines, what you may want to consider is to create a brief section, something like a paragraph, in the main body of document, not in the preface, to specify the search strategy used for this report. This could describe the time frame of the coverage, the search engine we use, for example, PubMed, MEDLINE, governmental

agency database, and so on, inclusion/exclusion criteria, search terms, and so on.

The other thing is that some of the -- there are some non-peer reviewed references. You mentioned one of them at the end of your slides, I guess. But there are other non-peer reviewed references that are cited and discussed in this report. I bring it up, because you state the literature summarized and referenced in this document covers the relevant published report for 1-BP. Well, technically those reports are not published, because they haven't undergone peer review. Although, there's a mention that a panel has evaluated a couple of these unpublished report. Again, inclusion of a search strategy section can be helpful, because it allows you to address issues like this and specify your inclusion and exclusion criteria.

PANEL MEMBER BLANC: Can I interrupt for a second. Could whoever is doing the technical, take down the slides, so that everybody sees your -- sees the speakers. We don't need to see the slide that says questions.

Thank you.

PANEL MEMBER BESARATINIA: Are we good to go?

Okay. Regarding the content, page two, I think it's line 93, it reads that in 1-BP treated males, the low

incidence of these tumors resulted in no significant difference relative to controls. And no significant positive trend was found.

And then two lines down -- I'm sorry, four lines down, it says the NTP concluded that the presence of these tumors in exposed females and the low historical incidence in controls indicated the tumors in males were exposure related. Well, these two sentences do not agree with one another. On the one hand, you're saying that the tumor incidence in the treated males is not different from that in control. And on the other hand, you're concluding that the tumors detected in the males are due to exposure to 1-BP.

Well, it's unclear to me if you are rephrasing the statement by the NTP or you're coding the original statement in the NTP report. Either way, the two sentences statements are not consistent with one another.

Also, on the same page, it reads -- I think this is also something you mentioned in your slides, that skin tumors of epithelial origins were increased in exposed male rats, and you cite Table 1, which is on page five.

Next page, on page three, top paragraph reads, "When combining all neoplasms of epithelial origin, the tumor incidence of keratoacanthoma... -- I can't spell this -- "...keratoacanthoma, basal cell adenoma, basal

cell carcinoma, or squamous cell carcinoma in males was significantly increased in all exposed groups and a positive trend was observed (Table 1)". And then, "The incidence of all epithelial tumors combined in all exposed group exceeded the historical control range for inhalation study. The NTP concluded that the increased incidence of all tumors of epithelial origin were a result of BP exposure".

Well, looking at Table 5 -- Table 1 in page five, there is no increase in the incidence of three out of the four tumor types of epithelial origin in the treated animal versus control. This include no increase in the incidence of basal cell carcinoma, squamous cell carcinoma, or basal cell adenoma in males treated with 1-BP versus control nor is there any trend in these animal. Just take a look at the P values there.

Only increases in the incidence of keratoacanthoma in two out of the three treatment groups that is 125 and 500 parts per million 1-BP are statistically significant. So the data in Table 1 do not really support the conclusion as it's phrased or written in page three.

What is also not clear is the rationale for pulling together the tumor incidence data for four different tumor types benign and malignant, and using the

combined values to reach this conclusion. This becomes more of the concern when on page 26, I think it's line 758. It reads that, The tumor -- The tumors OEHHA identified as being suitable for cancer potency determinations were adenomas of the large intestine in female rats the combined skin tumors of epithelial or origin male rats, including keratoacanthoma, basal cell adenomas or carcinoma, squamous cell papilloma or carcinoma, and so on.

Well, first of all, keratoacanthoma is benign lesion which rarely ever progresses to a squamous cell Carcinoma. As a matter of fact, only less tan six percent of keratoacanthoma become cancerous and progress to a malignant form. So I'm not sure about the justification for lumping together a benign lesion with rare potential to become cancerous with other malignant and non-malignant lesions in order to make a cancer potency determination.

I think I'm going to stop here. But all in all, I think most of these can be addressed by rewriting and revising the text, and rephrasing some of the statements that are made.

Thank you.

CHAIRPERSON ANASTASIO: Thank you, Ahmad.

Daryn, did you want to address any of Ahmad's comments now?

DR. DODGE: Yeah. Well, usually our derivation -- of to get to cancer slope factors, you know, tumors that are similar are combined and that's just a part of the process. And it's -- I guess, it's kind of a conservative way to look at developing a cancer risk factor or potency factor, but this is how we decided to do it in our -- in our branch here, OEHHA -- for OEHHA, our Cancer Unit Branch.

DR. BUDROE: I'll also note, I don't have the NTP document in front of me, but it may well have been that NTP considered all those skin tumor types to be related and to progress -- have the potential to progress through malignancy. And so they would have had essentially a bundled incidence in the NTP report. But we'll go back and check on that and see if we need to rephrase what was said about those rat skin tumors or not.

PANEL MEMBER BLANC: My interpretation of the comment of the lead would be that you could address this simply by a sentence that said that this kind of grouping is consistent with previous precedent and policy, just so that you acknowledge it. I don't -- I didn't hear of a critique as being that you should therefore not consider the bundled epithelial benign and malignant incidence, but simply that you need to put that statement in there just to make clear that this has been our established policy.

PANEL MEMBER BESARATINIA: Yeah. If this is a common practice and conventionally it's being done like this, that's fine, but probably a clarification, as Paul mentioned, statement would take care of that.

DR. BUDROE: Okay. We'll go ahead and do that.

CHAIRPERSON ANASTASIO: Great. Thank you, John. Thank you Daryn.

Daryn, anything else related to Ahmad's comments?

DR. DODGE: Yeah. If Ahmad could send us the studies he found, we could look at them and consider summarizing them in the report. You know, the more recent ones that he found from the late 2020-2021.

PANEL MEMBER BESARATINIA: Sure. I can do it and I think you can also follow up on it. I have a select number, probably six, seven papers, but there are more. You can simply go through PubMed. But I will send it -- how do I do that, Cort? Shall I send it to you or John or --

CHAIRPERSON ANASTASIO: No. Go ahead and send it directly to John.

PANEL MEMBER BESARATINIA: Okay. I'll do so.

CHAIRPERSON ANASTASIO: Yeah. Thank you, Ahmad.

DR. BUDROE: And we'll also take a second PubMed look.

PANEL MEMBER BESARATINIA: Yes. Thank you.

CHAIRPERSON ANASTASIO: Okay. Great. Thank you very much, Ahmad, for your comments.

I move now to the second lead, Karen.

PANEL MEMBER MESSER: Okay. Well, thank you, Ahmad. And I want to follow up by congratulating Dr. Dodge on a very well written report. I also found it well laid out. The accumulation of evidence seems clear to me. It was well documented. It was easy to understand. So I thought it was a high-quality report and I appreciate how easy it was to follow.

My comments, I'll start with an overall comment related to Dr. Besaratinia's latest comment, which is I think it's a strength of what's done here in the two reports that I've seen, that these reports generally follow well-documented policies. And wherever you can point that out, I think it's a strength and it helps to strengthen the weight of the evidence.

For example, this is a great example where you're combining epithelial tumors. When I read that, I thought, oh, that does seem reasonable. You know, adenomas progress to carcinomas. I take the point that Ahmad rose of these keratoacanthomas. I Googled them, because I wasn't familiar with it and they do seem to be rare in humans. I accepted that maybe they're less rare in rodents and maybe there's some evidence linking them to

cancer. But I think the fact that this is a policy decision undertaken before the report is written really strengthens the evidence base, because that, of course, means that you're not changing your analysis plan as you go through the report, that you have a procedure that's documented that you're following and you're letting the chips fall where they may as your analysis follows this procedure. So that's just a general comment. Wherever you are following a procedure, it's great to call that out and document it to whatever policy documents you have.

My -- the things that I might contribute to this discussion are also clarifications in methodology, and they're statistical, because that's my particular expertise. Generally, I found the statistics to be appropriate and well explained, understandable. I just had two areas where there might be questions on review, if this were a paper that were being reviewed in the scientific literature.

I thought the use of Cochran-Armitage trends in Tables 1 and 2 was a strength. So I think that is a good addition. Evidently, the underlying publication from 2011 produced these data and did these pairwise comparisons of each dose group to control, which is appropriate. But it's much more powerful to do a test for trend, a test -- dose response test, which is appropriately carried out

using this Cochran-Armitage trend test. So I think that's a strength and an appropriate addition.

I just want to make one technical comment, which is the pairwise comparisons are done using a small sample approach, Fisher's exact test, which is conservative. It gives P values that are too large, but you know that the type one error is appropriate. The Cochran-Armitage trend test is a large sample test, so it relies on asymptotics for its P values. However, it's robust. So I just wanted to add that to the comments that you might make or your policy documents that you might cite that this test is known to be -- you know, sample sizes are not that small. You've got on the order of 40 or 50 animals in the denominator across three different doses, but the numbers of tumors are small, so the probabilities are small.

So you're near the boundary of where asymptotics are well established. However, this Cochran-Armitage test is appropriate in this case, particularly if you're using equally spaced weights in the test. So pardon me for getting rather technical here. The weights were not described. So I think it would -- it would help you to say what the weights in the test were. Are using the dose levels or are you using an ordinal weight, zero, one, two, three? If robustness is a question, then it is more robust to use ordinal weights, zero, one, two, three.

In any case, these P values are very small. So I don't think it's an issue in this report. I can just imagine borderline cases where it might be more of an issue. And I could give you a citation to the big text book for discrete data analysis that would support these comments. I'm happy to do that.

The other technical comment is again more of a policy issue. This is a little bit more general, so maybe a little bit more of interest to other reviewers. You know, when looking at these tables, many, many comparisons are being made. And so there is the issue of multiple comparisons that comes to the front. And I think -- and it would -- again, I don't think anything inappropriate has been done here. I think there's a weight of evidence that's appropriately summarized. But I think the multiple comparisons issue, it would strength these reports, if the multiple comparisons issue was acknowledged and addressed with some policies.

What I might recommend, for example, for Table 1 -- should I share my screen to make it easier to follow? Would that be appropriate or...

CHAIRPERSON ANASTASIO: Sure, that's fine.

PANEL MEMBER MESSER: Okay. And I'll try not to go on too long here. So here's Table 1. I hope you can all see it. The issue is that we've got all these

comparisons within skin, right. We've got one, two, three, four, five different lines within skin. And within each line, we've got one, two, three comparisons against control, and then a trend test against control. So we've got quite a number of comparisons being made. And, of course, the family-wise type one error accumulates in this case. So that should be addressed.

I would suggest having some kind of multiple comparisons procedure within a group like this. I think combining them and then doing a trend test is a principled and power -- likely powerful way, an appropriate way to address the accumulated evidence.

So you might -- you might just think about this issue and maybe prioritize one test within a group like this as your primary standard-bearer. It seems there's an informal way of weighting the evidence to say that there was a statistically significant result across all exposure groups. I don't find that inappropriate. I just might think it through and formalize it a little bit more. So generally, what you can do is you can institute a formal multiple comparisons procedure on a hierarchy or a few tests and then have a policy for looking for a weight of evidence across uncontrolled multiple comparisons.

And again, the suggestion is just to acknowledge the issue and think about some appropriate policies. It's

not a suggestion that there's any real underlying weakness here, because I think it seems that the weight of the evidence has been what's driving these conclusions and it seems appropriate to me. So it's just a general recommendation to consider the multiple comparisons issue and write some policies down.

My only other comment -- I have some minor comments. Let me find my notes. This is my ignorance. Please excuse me. The computation of your constant C, capital C, and I didn't note the page, but this is where you're going from like 6.2 hours up to annual exposure. I didn't quite follow it. That's just algebra, but I didn't quite follow it. I got left at a weekly exposure not an annual exposure. So if you could just please double check what you wrote and make sure it's correct there.

If you could please clarify that the lower confidence limit from your EPA models -- I had to think about this. On Figure 2, thank you for that figure. It's very clear. It helped me understand what's going on. And thank you for pointing out on page 33 the sentence where you say linear extrapolation from the BMDL to the origin was used to determine the slope. That was very clear. That helped me understand how you're using the model. The only thing I would have liked was to understand that the BMDL itself came out of the software.

So I understood that the -- you know, the BMD came out of the software. I would have liked to have had a note that the BMDL came straight out of the software. I was trying to figure out where that came from.

And then let me just go back. Yeah, those were really my comments. The only other thing is -- yeah, on the Cochran-Armitage test, please indicate the software used and especially the choice of weights or scores for the categories. So I can send you these technical comments in a written form to make them easier to follow.

Thank you.

CHAIRPERSON ANASTASIO: Thank, Karen. Yeah, I think that would be very helpful to send the technical comments in a written form.

Also, are you available for statistical consulting --

PANEL MEMBER MESSER: Sure.

CHAIRPERSON ANASTASIO: -- for comparison issues should OEHHA have questions?

PANEL MEMBER MESSER: Absolutely. No problem.

CHAIRPERSON ANASTASIO: That would be great. Okay. Thank you very much.

Well, great. Thank you very much, Ahmad and Karen. I'd like to now open it up to the Panel at large.

Yes, Paul, go ahead.

PANEL MEMBER BLANC: Okay. I'll try to figure out how to take my hand down too. My first question is in regard to your comment on using survival time or time till tumor incidence, which you only invoked for the study where there was high mortality at the highest dose level. But when you showed the data on the tumor incidence per surviving animal, I noted that the -- there was no loss of survival in the analysis of the lung tumor incidence in female mice, which ultimately was the endpoint you used to derive the cancer potency factor. My interpretation of that, because it was so different from the others, was that, in fact, the tumor in -- the tumors was -- were happening early enough that the mice weren't dying from another factor.

And if that's correct, wouldn't it make -- would it be more powerful to use time until lung tumor incidence as your endpoints, since they seem to be developing the tumors earlier relative to other things that are happening? In other words, most of these skin cancers are being detected when the animals are sacrificed, but a lot of the animals have died for other reasons, that's why the N is smaller. But maybe I'm misinterpreting the implications of those data. So I think it would -- for me, it be would be better to have them answer the questions as I bring them up.

CHAIRPERSON ANASTASIO: Yeah. I think that's good.

Daryn.

DR. DODGE: Thank you, Dr. Blanc. Yeah. Well, we'll discuss this with our statisticians in-house here about this. Basically, it didn't quite meet the criteria to use a Weibull time-to-tumor model. So that's what I can say generally. So we just used the general multi-stage model.

PANEL MEMBER BLANC: I mean, I'd be curious what Karen might have to say about it, whether I'm overreaching in terms of what those data implicate.

PANEL MEMBER MESSER: Well, I think that's an interesting observation that didn't come to my mind, that the lung tumors must be occurring earlier. And certainly a time-to-tumor model has more power. But I -- again, I think that the general comment is that if there's an established policy to address this issues to say when you switch from one model to the other, that's a real strength, and that policy should be followed.

PANEL MEMBER BLANC: And sometimes we have presented the results of the alternative method just to show that it doesn't really substantively change the results and that can be very useful, too, Daryn.

PANEL MEMBER MESSER: As a -- as a sensitivity

analysis.

PANEL MEMBER BLANC: Yes. A kind of sensitivity analysis.

PANEL MEMBER MESSER: And again, I would just urge that there be a policy for when that's appropriate, with it's not, so no one can be accused of cherry picking.

PANEL MEMBER BLANC: And then my other comments are sort of entirely different nature. The date -- the mutagenesis data suggested that, in fact, this is a -- this may very well be a chemical which acts without requiring metabolism. And for that reason, it was somewhat distracting to have so much about the metabolite that can be used as a biomarker. I guess -- and especially, if what it was meant to do was show you can widely detect this biomarker, but we actually don't know if it's a specific biomarker to this parent compound.

So I wouldn't change your -- it doesn't affect your cancer potency piece of the document. But I certainly would have appreciated a little bit more -- it was like an aside in that section, you know, that maybe this doesn't require metabolism at all. It's a direct acting carcinogen. And that certainly has implications. And to me, it would have some implications also for a chemical, which is largely excreted unchanged throughout exhalation, which means that the lung is being exposed

coming and going, which, of course, would make the choice of the lung tumors all the more rational. So there were some implications to that that weren't discussed.

And also, I thought what got lost was the fact that this chemical is debrominated. You kind of alluded to it in your discussion where you said that, you know, this brominated by-product is a -- is a known carcinogen. But all of that, that figure of the metabolism, you know, I looked at it and I said, well, where did the bromine go and what is the implication of having a de-brominated piece of this circulating of the body? Is it bromine itself? Has it been oxidized to something, other bromine? Is it -- you know, I just wanted to know, because bromine -- well, first of all, I was kind of surprised nobody looked at bromine as a biomarker. If it's being debrominated, you should be able to just measure bromine, which is not normally present in anything other than trace amounts in the human body.

So those -- this is not going to change your document in terms of your, you know, delivering the goods on a cancer potency factor. But it certainly would be clearer. I also think there was a point where you left animals and went to some human data and it was missing some kind of section marker that said human. All of a sudden, I was seeing children and adults. It was like

children and adult rats. What is this? So that's just put in a -- you know put in a section there.

Those are my comments. And of all of them, I think my question about the time until tumor is probably the most substantive, because that would affect your cancer potency calculation.

CHAIRPERSON ANASTASIO: Okay. So Daryn, I know you addressed the time-to-tumor approach. Anything else you want to say about that?

DR. DODGE: Yeah. Thank you, Cort.

Yeah. We will discuss our policy and why we chose one model over another regarding the female mice there. Regarding the bromine, bromine is released during metabolism. And it does circulate in the body. It did -- what -- my impression from reading the metabolism studies of 1-bromopropane is that workers have to be exposed to relatively high levels of 1-bromopropane in order to measure -- to reliably measure an increase in bromine that was due to exposure to 1-bromopropane. So it wasn't as good a biomarker as the -- n-acetyl-s-propylcysteine in urine.

PANEL MEMBER BLANC: I think you can say that in one sentence. And you could also say in one sentence that bromine is not considered in and of itself a carcinogen, if that is truly the case, because those are questions

which obviously arise. And what you don't say, it just leaves the -- it just leaves it as a kind of open question.

DR. DODGE: Okay. Thank you, Dr. Blanc.

Yeah, I'll emphasize that. We did cover some of the studies that looked at bromine levels in urine in these workers, but I -- I'll emphasize that overall it was thought, at least for non-occupational exposure, it may not be a good marker, because it's hard to detect levels above what's normally in the bromine levels in urine.

DR. BUDROE: One thing I'd also like to note, as far as some of the discussion about policies, methodology policies, early in the document, we usually refer to the cancer potency technical support document. And that's a document that the Panel has approved and it contains essentially a description of most of the methodologies that we use in generating cancer inhalation unit risks. So, I mean, we don't go into detail quoting from the methodology document, you know, for the sake of parsimony.

But it's -- you know, we do have a published methodology that you can refer to.

PANEL MEMBER MESSER: I might suggest citing it more frequently, whenever there's one of these issues. Just feel free to cite it.

DR. BUDROE: Okay.

CHAIRPERSON ANASTASIO: All right. Thank you, John.

Let's move on to Joe.

Joe, you're muted.

PANEL MEMBER LANDOLPH: There. Thank you.

Yeah. I appreciated reading the document. I agree with Karen and Ahmad. It was written, in general, very well, very clear. And it looked like they had a literature -- good literature search on the earlier years. I agree with Ahmad's comment that it's very important to do the latest years you can get. I think the genetox database is somewhat thin for this compound. And the metabolism clearly indicates it looks like it's going partly by P450, partly by glutathione conjugation and breakdown of imines and other reactive metabolites. So clearly more work needs to be done on this compound to make it a really solid study. And that's not OEHHA's fault or SRP's fault, just we need more data on it.

So I would say I looked at this as a regular old review and I wrote a review. I'll send up a few comments -- small comments on the English and a few on the genetox database to help you out. And I appreciate all your efforts, and energy, and expertise that's went into this. And I'll try and help you strengthen it just a tiny bit more.

Thank you.

CHAIRPERSON ANASTASIO: Great. Thank you, Joe.

Mike.

PANEL MEMBER KLEINMAN: I just have a few additional comments. One of them may be the way these documents are structured. But it seems to me that the preface, which is, you know, in the Roman numeral pages from the intro, is where you give a lot of introductory material about the compound, how it's used, the background for the Hot Spots Program, et cetera. And I'm wondering if that couldn't be relabeled as introduction and moved into the main body of the report, because I think people tend not to look at those preface pages as being part of the information being presented. And, you know, that's where you also talk about how this material is used and the various kinds of applications. So there are a lot of consumer product uses and things like that. So there is, you know, a potential for exposure.

The information in Table 1, which is, I guess, directly out of the NTP report, later you actually take these data and convert them in your Table 5 or 5A using the adjusted tumor incidences. And I'm wondering whether that should be, you know, mentioned in the discussion of Table 1 that you actually use that, because the adjusted tumor incidences actually gives you, you know, stronger

trends and somewhat different P values for the doses. And I think the adjusted tumor incidences are probably more relevant for -- yeah, for your analysis.

The other thing that I thought was -- it might be useful, at least from the toxicology standpoint is adding the bromine stripping, you know, at least in the flowchart of metabolism in Figure 1. We know that the bromine is coming out. It's probably coming out as radicals or as possibly HBR. And there is some indication in the literature that the bromopropane leads to irritation and possibly inflammatory changes in the respiratory tract, which are not germane, given the cancer potency, but might be useful for people to know that it is an irritant and probably due to the hydrobromic acid that's released in the lung or in lung tissue. So I think adding just that -- you know, showing the bromine coming off would make Figure 1 more complete.

Other than that, I think this has been -- this is a very well written report and make -- you know, I think it's a very good addition. The -- I did get some indication that U.S. EPA is -- either has designated it or is possibly -- is contemplating adding 1-bromopropane to the list of hazardous air pollutants. So I haven't followed up on that, but it might be worth double checking and adding that to the introduction if that is the case.

Other than that, I think this is a very good job. Thank you.

CHAIRPERSON ANASTASIO: Okay.

DR. BUDROE: Okay. And, Dr. Kleinman, one thing I want to note about the document structure is that the document is written so that essentially the part after the introduction can be put into Appendix B of the cancer technical support document. So that following section of the document fits that format, where most of the other they're essentially summaries. What goes into Appendix B is essentially really a summary of the whole document. So that's why the preface, the introduction that will not go into Appendix B, because it doesn't fit the format.

PANEL MEMBER KLEINMAN: Okay. Thank you.

CHAIRPERSON ANASTASIO: Thank you, John.

Beate.

PANEL MEMBER RITZ: Yeah. So I really enjoyed reading this. Thank you for all your work on this document. I was quite surprised to see that 99 percent of the NHANES population and also that women -- pregnant women population had actually the metabolite in their urine and as measure. And then the documents says while we are not sure that the general population is actually exposed because this metabolite is not all that specific. But I couldn't really get how we could get to a 99 percent

detection rate, more or less, for this metabolite if it's not in the general environment. And I think that's not what the document really helps us understand currently, how the general population would be exposed.

So would it just be at hot spots where you're living near a facility and, you know, it's gassing off, and if you're closer to the facility maybe as a general community member you're exposed or would it be also in products that are in the home, in the laminate, or in the foam, or is that not the case? That I would -- I mean, if we're talking about population exposures, I think it would be worthwhile explaining that a little bit better.

DR. BUDROE: Okay. I -- Daryn, do you want to speak to that?

DR. DODGE: Yeah. I -- you know, I looked into this to try to figure out, well, what are these -- what are these individuals being exposed to and I couldn't come up with much. I don't have any other ideas about what could lead to this particular metabolite. And U.S. EPA in their review didn't really have anything to say about that either, except that there might be something else other than 1-BP that's resulting in this particular metabolite in urine.

But I can dig a little deeper and see, because I'm kind of interested in knowing as well why it seems to

be -- there seems to be a widespread exposure, you know, low levels, but still widespread. You know, the other thing I want to say is that, you know, in the worker studies where they're actually working with 1-BP, there is a really good association between urine levels of this metabolite and exposure. It's just it hasn't been done for the general population, the non-occupational.

PANEL MEMBER RITZ: Right. And, I mean, I didn't read those worker studies. Sorry. But did you see anything that also suggested that gassing off in the vicinity of the company or people who weren't directly working with the agent had the metabolites in the urine as well or only the workers who worked directly with them?

DR. DODGE: There -- you know, I can't -- I haven't been able to find any studies that looked at exposure to people living near facilities that are using this compound. There -- you mentioned earlier there could be consumer products that have 1-bromopropane in it and that could be a possible reason, you know, at least partially why the numbers seem to be so high for exposure in non-occupational situations.

CHAIRPERSON ANASTASIO: Daryn, do you think any of the halogenated propanes are going to give a similar metabolite, right, because it's just the propyl group that adds to n-acetylcysteine.

DR. DODGE: Yes, that could be. That -- some of these other brominated compounds that I mentioned that had been looked at in toxicology studies, they were only one or two carbon chains. There are -- you know, there's one three-carbon, but, yeah, I'm not sure what other compounds could result in this particular metabolite.

CHAIRPERSON ANASTASIO: Yeah. So maybe integrating across a whole family of brominated alkanes, yeah.

DR. DODGE: I will add that in one of the biomonitoring studies they did not find an association between cigarette -- secondhand cigarette exposure and these 1-bromopropane levels in the -- in the people. So it doesn't appear to be anything in cigarette smoke.

CHAIRPERSON ANASTASIO: Okay. Thank you.

Karen, do you have a comment? Oh, sorry. John, did you want to say something about that?

DR. BUDROE: Yeah, just that it's entirely possible that 1-BP was winding up in consumer products or in things like, you know, construction foam and remanufactured housing or something like that, and they're just, you know, not making an effort to inform everybody that they're actually using 1-BP in those products or applications. So that's kind of bad input data or no input data.

CHAIRPERSON ANASTASIO: Yeah. Karen, do you have a comment?

PANEL MEMBER MESSER: Yeah. I was struck by the high prevalence of this biomarker across the population. I thought -- but I couldn't find anything in the report to put into perspective the level. You know, it seemed to be about three nanograms per milliliter for these kids and pregnant women. And I didn't know whether that was really low or where it sit -- sat on the spectrum of the occupational exposure study. So if that kind of perspective is available, that would help.

CHAIRPERSON ANASTASIO: Yeah. Thank you, Karen.

Kathy.

PANEL MEMBER HAMMOND: Yes. I think in general my comment relates to the exposure -- or the lack of exposure data in this. I just did a quick -- this is just Wikipedia. It says that its use has been increasing in the 21st century resulted from the need for a substitute for chlorofluorocarbons as a dry cleaning solvent. However, it's use in dry cleaning has been steadily declining and it was nearly obsolete by 2020.

I just think that we do need to understand the exposures. I think particularly looking at what were the environmental levels compared to the occupational levels and what has been seen there. So, yeah, I wasn't sure why

there was not more in the occupation -- in the exposure area in the -- in the report, because that puts this into some context as to how important it is and how it is that people would be exposed.

CHAIRPERSON ANASTASIO: Right. Daryn, yeah, I remember there was no ambient concentration data, but I can't remember if you addressed that and there's just no data available. Could you say something about that?

DR. DODGE: I think I alluded to that in the report, but I can certainly emphasize that a little better.

CHAIRPERSON ANASTASIO: And there is no data available for ambient concentrations?

DR. DODGE: Not as far as I know, but we can take another look.

PANEL MEMBER HAMMOND: And NIOSH does have a hazard alert on this, right?

DR. DODGE: I'm not sure of that.

PANEL MEMBER HAMMOND: They do.

DR. DODGE: Okay.

PANEL MEMBER HAMMOND: I'll make that as a positive statement.

DR. DODGE: Okay.

CHAIRPERSON ANASTASIO: All right. Thank you, Kathy.

Any other comments?

PANEL MEMBER KLEINMAN: This is Mike. I just was wondering whether it would be useful to increase the list of comp -- you know, the ways in which this compound is used industrially. One of the ones that I noted was that it's used in the production of asphalt. And almost all of us have been out there on the street exposed when roads are being tarred and that sort of thing.

So there's a lot of opportunity if this stuff off-gases during that heated period for people to get, you know, some exposure. So it might be good to just expand the list of uses so people have a better idea of where they might be exposed.

CHAIRPERSON ANASTASIO: Okay. Thank you, Mike.

Karen.

PANEL MEMBER MESSER: And I thought there was an opportunity to put the exposure levels in context against the cancer risk. I don't know. Maybe this isn't something that's usually done in these reports. But if -- you know, the occupational exposure data that was there that was 460 milligrams per meter squared for sprayers, you could translate that into an increased cancer risk. And it's using the final model and it's not insignificant. So I thought that was an opportunity to say, yeah, there -- there are potential exposures that might be

important.

CHAIRPERSON ANASTASIO: Daryn, do you want to say something about occupational versus environmental exposures?

DR. DODGE: Yeah, I don't think we've done that in these documents before, but we might be able to add something to that effect.

PANEL MEMBER MSSSER: Then maybe it's not appropriate. It just did seem to me that occupational exposures are in an important range.

DR. BUDROE: Right. That starts to get into Cal/OSHA territory. So we -- technically, we're not involved with, you know, standards or even, you know, associating exposure and risk for workers.

PANEL MEMBER MESSER: Okay.

CHAIRPERSON ANASTASIO: Paul.

PANEL MEMBER BLANC: Yeah. A couple of comments. One, about this topic, I would say that the other comments that you've received about clarifying the metabolism pathway and emphasizing that this is debrominated is helpful to contextualize the metabolite, which actually isn't specific to this compound. By definition, it doesn't have bromine in it. So in terms of the theoretical possibilities of what this biomarker represents is contextualized better by emphasizing that.

But my main question is a completely different topic and touches more on our generic approaches to things. As you point out very clearly, you're using for the rat models a formula that was developed by OEHHA in 2018, but that for mice conversion you're using a 40-year old formula.

And so this is a question not about this document nor anything that I'm suggesting you change. But is the reason why we never developed an OEHHA-specific formula because we more likely than not tend to use rat data and not mouse rodent data or is it because the feeling was that the formula from 1988, or '83 - maybe it was from 83 - is -- still holds up and doesn't need to be revisited?

DR. BUDROE: Hey, Daryn, I think I can speak to this one.

DR. DODGE: Yeah. Thank you.

DR. BUDROE: Yeah. The 1983 equation was actually developed by U.S. EPA. Anderson et al. was a U.S. EPA research group. And we went back, we updated. There were sufficient new data sets in rats to be able to correlate inhalation rate with body weight that we were able to develop a different rat breathing rate equation. We looked at the mouse data and there weren't enough new good data sets to be -- to go ahead and redo, essentially

supplant, what Anderson already had put out there. So it's a question of, you know, what data is available to work with in the literature. And for mice, there just wasn't enough new data to work with of sufficient quality.

PANEL MEMBER BLANC: Okay. Well, that's helpful. And maybe this comes back to that question about what's in our policy document and what's not. And as long as you guys are on top of it, so that if such data do develop, you do do that exercise, I think I, from my part, would be supportive of that. And because it is a little bit of disequilibrium there to have one thing updated, you know, three years ago and another one that's 40 years old.

CHAIRPERSON ANASTASIO: All right. Thank you, Paul.

Kathy.

PANEL MEMBER HAMMOND: Yeah. First, I would say I do think it's relevant that -- I know that Cal/OSHA is in charge of regulations, but the point isn't to -- that you -- that means you can't talk about occupational exposures. I think the point is to understand what the occupational exposures are and compared with environmental exposures.

Also, it's -- a quick little Googling here, I see that it's used in some cleaning products in the home, so that might be one of the reasons that it's showing up in

the general population. And if -- you know, I -- this is a quick thing and it needs to be done more thoroughly. But if that's true, I think that's worth mentioning. I mean, I would follow that up a little closer and make sure that's still true. But, that looking -- it's used in two -- at least two consumer products, so --

CHAIRPERSON ANASTASIO: Thank you, Kathy.

PANEL MEMBER HAMMOND: Yeah.

DR. BUDROE: Okay.

CHAIRPERSON ANASTASIO: Lisa, anything to add?

PANEL MEMBER MILLER: I'm sitting quietly listening to all of this. The main takeaway for me, and I can't add anything technical to this, but what struck me is -- related to the comments that several of the Panel members brought up is the lack of perspective in terms particularly in exposures to the general population. And I think this is important in -- I understand the issues with the occupational exposure component. But the issue here is that at this point in time, we don't see evidence of development of cancer in the human population most likely due to the duration at which this product has actually been -- has been out there in terms of exposure. So because of that, I think having that information on what people are being exposed to, whether it's, you know, ambient or whether it's occupational.

One of the things that I think Mike brought up very briefly in terms of the respiratory response, the inflammatory response, when I did a quick skim of PubMed, it's -- it was clear to me. There aren't a ton, but there are some studies reporting symptoms associated with inhalation, both dermal and respiratory symptoms, and again, I think they may be, you know, due to some of the chemical actions of this -- of this compound once it is released into the air.

But that said, I think having the dosimetry information, in addition to what's provided, I think it's -- what I could skim from the document was that there is one study that is presented and maybe it's because it's perhaps the most high quality study that you were able to identify. But it would be helpful to gather as much relevant dosimetry data that is available and provide it, so that the reader gets some perspective on what -- you know, what individuals, whether occupational or unoccupational exposures, are going through, because again, it's sort of a wait and see at this point in time.

So I think it would -- it would strengthen the data that have been obtained so far from the animal studies.

CHAIRPERSON ANASTASIO: Okay. Thank you, Lisa.

I just had a few comments. One was on page one,

you know, so this is a very volatile chemical. And the animals are exposed to aerosols, right? But those aerosols must have evaporate pretty much immediately. So I'm wondering if they had good control on their actual exposures on the gas phase concentrations that the animals are exposed to.

I'm looking at you, Daryn.

(Laughter.)

DR. DODGE: Okay. I was writing down your question.

CHAIRPERSON ANASTASIO: Oh, sorry. Feel free to finish.

DR. DODGE: Yeah, well, you're talking about the NTP study, is that correct?

CHAIRPERSON ANASTASIO: Yeah. This is on page one -- let's see, dah, dah, dah, dah. Yeah, it's the NTP study. You know, you talk about a uniform aerosol concentration, but I feel like for a volatile -- a very volatile species, it's a little counterintuitive to talk about an aerosol concentration. I understand that's the generated aerosol, but it must immediately evaporate.

DR. DODGE: Yeah. You know, I -- they go into pretty -- a lot of detail on their methodology on how they generate the aerosol or gas. I can clarify that in the report what they're actually measuring.

CHAIRPERSON ANASTASIO: Okay. Yeah. It would be helpful maybe just to -- you know, when you -- maybe just to clarify, it's initially applied as an aerosol, but it's expected to be immediately evaporate and give the reader some confidence that they actually measure gas phase concentrations or have some understanding of what the actual gas phase concentration is.

DR. DODGE: Okay. Yeah, I can do that.

CHAIRPERSON ANASTASIO: The other comment I had was, you know, you talked about these kind of comparison structures of small bromoalkanes. I don't know if there are inhalation unit risk factor values for some of these other compounds. But at the end when you show the IUR of 1-BP, it would be nice to compare that to some of these other structures. Just give us a sense, are they similar in terms of cancer potential or are they wildly different? Just for me, it would have given me a little closure on that question.

DR. DODGE: You know, that is a good question. Two of the compounds that I mention in there that are similar to 1-bromopropane, I believe are actually oral studies or gavage studies, two-year studies. So it's -- it may be a little difficult to compare to an inhalation study.

CHAIRPERSON ANASTASIO: Yes. Right. Yeah, it

would have to be an inhalation study for the comparison to be meaningful, I think.

DR. DODGE: But they did result in similar types of tumors, whether it was for orally administered or inhalation.

CHAIRPERSON ANASTASIO: Yeah. Okay.

Well, if any of them had inhalation exposures, the resulting IURs would be helpful, just for comparison.

DR. DODGE: Sure I'll make sure of that.

CHAIRPERSON ANASTASIO: Okay. That would be great.

Two other minor comments. One is I really appreciated the quick explanation of terms for those of us who are not toxicologists, having a one sentence description of what it is a micronuclei or whatever else. That was really helpful, so thank you for doing that. And I really hope you guys will continue that moving forward.

And then also this is something Beate brought up a while ago, you know, not just putting the asterisks for P less than 0.05, but it was very helpful to have the P values in the table. So thank you for doing that again. But it just helps understand how close are you to different levels of significance.

Okay. So any other comments on 1-bromopropane?

Seeing none. I'd like to thank Daryn and OEHHA

for the document and for bringing it to us today. Obviously, there was wide spread agreement. It was -- it's a good document and it's a good IUR value. With that, we're going to move into a short break time. So I currently have 11:18. We're going to take a 10-minute break. So we will reassemble at 11:28. And I will see you then.

(Off record: 11:18 a.m.)

(Thereupon a recess was taken.)

(On record: 11:28 a.m.)

CHAIRPERSON ANASTASIO: All right. Welcome back, everyone. Panel members, if you can turn your cameras on, then I'll know you're with us.

DR. DODGE: Hi, Cort. This is Daryn. I'm here even though my camera is not working.

CHAIRPERSON ANASTASIO: Great. Thank you for letting me know Daryn.

DR. DODGE: Okay.

CHAIRPERSON ANASTASIO: All right.

So Joe. Mike and Ahmad, are you with us?

Mike, Ahmad, are you guys here?

PANEL MEMBER BESARATINIA: I'm back. Sorry, I'm back.

CHAIRPERSON ANASTASIO: Great. Thank you, Ahmad.

PANEL MEMBER BESARATINIA: Sorry.

CHAIRPERSON ANASTASIO: That's okay.

Mike, are you back? Well, okay, I am sure Mike will join us shortly, but I'd like to get started again. So the next, and second, and last major agenda item for us today is a discussion of AB 2588, the Hot Spots Emission Inventory Criteria and Guidelines Regulation.

So I just want to clarify something for the public. The Scientific Review Panel does not take public comments on health guidance values. So I couldn't address any comments that we received on the 1-bromopropane document.

On this upcoming 2588 topic, we will not be taking comments on the first portion, which is just a retrospective of what CARB has done related to updating Appendix A, but we will be taking comments on the second part of the 2588 discussion. And I'll talk a little more about that once we get to part two of the discussion.

So as a preface to part one of the discussion, the retrospective, just remind the Panel that starting in June of 2019, CARB staff updated us on AB 2588 Air Toxics Hot Spots Emissions Inventory Criteria and Guideline Regulation. And we had multiple meetings about the topic. And then, CARB worked with other stakeholders as well and then in November of 2020, CARB's Board adopted the proposed amendments to this program. So there are many

more substances now in Appendix A than there were before this revision.

In the first part of today's 2588 update, CARB staff is going to give us a summary of the amendment process, and then in part two, they'll discuss with us what to do moving forward and have several questions for the Panel to talk about how to move forward and future pathways. So again, after part two, we will open the floor to the public comment, but not for part one.

So Gabe Ruiz, who is the manager of CARB's Toxics Inventory and Special Projects Section in the Air Quality Planning and Science Division, is going to start us off with a presentation on part one and is going to give us a brief recap of the ICG amendment process.

So, Gabe, take it away.

(Thereupon a slide presentation.)

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Thank you, Cort. Good morning, members of the Panel. Good morning, everyone else. As many of you are probably aware, we recently took to our Board a number -- a number of proposed amendments to the AB 2588 Emission Inventory Criteria and Guidelines Regulation, or EICG. And in the course of developing these amendments, we had a number of consultation meetings minutes with you about our proposed revisions to the Appendix A chemical list.

Today, we have prepared a two-part presentation to provide you with a status update on the amendments to the chemical list and to share a prospective discussion that we hope will inform future revisions.

Next slide, please.

--o0o--

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: In part one of the presentation I will provide a brief recap of the AB 2588 Air Toxics Hot Spots Program, a summary of our previous discussions with the Panel and the recommendations you provided, and an update of the current status of the amendments.

I will then pause for, you know, some questions about the status so far. And then in part two, I will go over our proposed plan for a five-year review and update cycle, and we'll present some questions that we would like to pose to you about the process. I will then -- I will then end with a brief overview of the next steps.

Next slide, please.

--o0o--

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: The Air Toxics "Hot Spots" Information and Assessment Act, also referred to as AB 2588, was signed into law in 1987 to address public concerns about potentially significant exposure to air toxics emitted by

facilities.

The Act established a public right-to-know program by creating a process to collect data about toxics emitted from facilities and make it available to the public, identify facilities that represent a localized health risk, and outline a process for facilities to notify the public about risks and ultimately reduce those risks.

AB 2588 required CARB to develop the criteria and guidelines for developing facility toxic inventories. Among many of the requirements, the Act requires CARB to compile and maintain the list of substances that must be reported. And the statute identifies specifically what must be considered, such as CARB's own Toxic Air Contaminants, U.S. EPA's Hazardous Air Pollutants, and others.

The statute also gives CARB the authority to include other substances that may pose a threat to public health when present in the air.

Next slide, please.

--o0o--

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: During development of the recently approved amendments to the regulation, we engaged the Panel over a series of four meetings from June 2019 to February of

2020, in which we presented our proposed revisions to the chemical list and requested your input and scientific expertise in evaluating and validating our technical approach.

In October of 2019, after reviewing the initial list of proposed new substances, you gave us recommendations on additional chemicals that we should consider for addition to the list. In November of 2019, we provided an update on the substances we had added based on your recommendations and you provided additional guidance.

And then in February of 2020, you issued an interim findings letter conveying the Panel's support for the proposed revision to the chemical list.

Next slide, please.

--o0o--

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Some of the recommendations made by members of the Panel during our discussions included reviewing chemical lists published by the American Conference of Governmental Industrial Hygienists, or ACGIH, the National Institute for Occupational Safety and Health, or NIOSH, and the Olson Toxicology Handbook.

Additionally, you recommended that we consider adding aldehydes, isocyanates, freons, and other

fluorocarbons, as well as methylating agents, epoxides, strobins, and rare earth metals. The Panel also expressed support for our proposal to add three broad classes of chemical bays -- of chemicals based on their functional group. Specifically, these functional groups include isocyanates, poly and perfluoroalkyl substances, or PFAS, and halogenated polycyclic aromatic compounds. The Panel concluded that these functional groups can be reasonably expected to pose a threat to public health when present in ambient air.

In addition to seeking your input on the revisions to the EICG chemical list, OEHHA and CARB also made presentations on the concept of developing provisional health guidance values. These presentations noted that the process for developing peer-reviewed health guidance values can be very lengthy and resource intensive.

Since many of the new added -- newly added chemicals do not yet have peer-reviewed OEHHA health values, we propose the development of provisional health values that could be used as a screening tool to identify chemicals of concern.

The Panel expressed support for this concept and encouraged our continued collaboration with OEHHA to develop similar methodologies for developing provisional

health values.

Next slide, please.

--o0o--

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: So based on your recommendations, we added more than 100 substances from the ACGIH list and 20 additional NIOSH substances. We also added several individual isocyanates and rare earth metals, as well as a few methylating agents and strobins. Additionally, we added over 200 PFAS -- individual PFAS substances, in addition to the PFAS functional group.

Per Dr. Kleinman's request, we also added language to the regulation text to create a mechanism for public input in the nomination of new substances proposed for addition to the list.

We also initiated discussions with OEHHA staff on the development of provisional health values and tried to continue further discussions as part of the next steps.

Next slide, please.

--o0o--

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: So as you may know, our Board adopted the updated chemical list at the November 2020 Board hearing. We would like to thank Cort for testifying in support of the amendments and for conveying the support of the entire

panel for the work that we did in updating this chemical list.

At the Board's recommendation, we continued our outreach with stakeholders, which resulted in additional modifications to the regulation through what we refer to as 15-day changes. The most significant of these changes include an adjustment to the phase-in schedules for some chemicals and the addition of several individual PFAS substances. The original proposed could have a phased-in approach for new chemicals to create a more manage -- manageable workload for facilities and air districts. The phase-in schedule allowed for two phases with the first group of substances phasing in on the first year of implementation and the second group phased in four years later.

In response to concerns that quantification methods are not available for many substances, we moved several chemicals to a later phase. We also added several individual PFAS substances to the individual list of chemicals that must be reported if they are needed and include a PFAS target list that facilities in the wastewater treatment sector must test for as they develop their source testing programs.

The final regulatory package is now undergoing final review by the Office of Administrative Law. And if

everything goes as planned, we anticipate that the amendments will become effective by early 2022.

So next slide, please.

--o0o--

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: This concludes part one of my presentation. I would now like to open the floor for questions from the Panel about the process so far, before we launch into a prospective discussion in part two.

CHAIRPERSON ANASTASIO: Great. Thank you very much, Gabe, and also congratulations to CARB on this much needed update on the Appendix A. That's great to move that forward.

Panel members, comments on the retrospective portion of AB 2588.

Yes, Paul.

PANEL MEMBER BLANC: In terms of the list of 110 plus substances that you referred to, based on ACGIH, and NIOSH, and others, will you be circulating list to us?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Certainly. I think we can do that. We are working on a supplemental document. So you probably are familiar with, you know, the formal regulatory Appendix A. It includes, you know, things like chemical name, ID, source list, you know, whether it's a carcinogen or not, and a

few other pieces of information. We are working on a supplemental appendix -- or a supplemental guidance document that actually will include more information. And, yeah, we can circulate both the full list and also an abbreviated list that specifically updates the -- or states the substances that we're --

PANEL MEMBER BLANC: Yeah, I think what we'd like -- what I'd like to see is not the full list, but just the new ones that you're suggesting, because it would help us close the loop. Our discussion was more than two years ago, I think. And so I'm not even going to, you know, necessarily remember the things that we highlighted, but it would be useful to me as Panel member and I think to other, to see how our suggestions translated into concrete recommendations.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Okay.

PANEL MEMBER BLANC: You know, for example, which rare earth substances? I think it would just help us. And if -- and if any of us saw something that was like wait, how could that be there and not the other thing, we could give you early feedback.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Certainly. Thanks. And just -- I just want to remind you that we did -- as part of our, you know, update

process, we did kind of check back with you -- you know, members of the Panel regularly and provided updated documents. But yeah, it would be probably way too detailed, you know, for you to be able to see specific short list of ACGIH, but we will -- we will create that and forward that to you.

CHAIRPERSON ANASTASIO: Yeah. Just to remind Paul, you know, we did have multiple meetings about this. And at several points, we received spreadsheets with the new substances that were proposed. I don't remember if we ever got one at the end that had everything that we had in it, so that would be great, Gabe, if you could provide that.

PANEL MEMBER BLANC: Yeah. That's all. That's all. I'm not impugning anything.

CHAIRPERSON ANASTASIO: Yeah.

PANEL MEMBER BLANC: It just would be helpful to have that.

CHAIRPERSON ANASTASIO: Yeah. Other Panel member comments?

All right. Seeing none, let us think about -- oh, wait. Sorry. Mike Kleinman with a last minute addition. Mike, go ahead.

PANEL MEMBER KLEINMAN: Last minute. I just wanted to raise the issue, PFAS was mentioned. And we

should remember that there are something like 9,000 different PFAS- and PFOA-type compounds that are continuously being added to the list of chemicals that are being used industrially and in other applications. So as we start thinking about that as a group in some way trying to understand how to characterize those or categorize them may be very important going forward.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yes. So one of the things that we did was, you know, as I mentioned the entire chemical group, so any substance that has a PFAS chemical group or that it can be classified as a PFAS, if it's emitted by any facilities in the State, then they have to report it.

We also understand, you know, there's a lot of times not a -- there's no methods to quantify those emissions yet or even to detect in the air. So we did allow for, you know, some provisions that facilities that use or produce these chemicals, we're going to have to -- please let us know how much they're using, how much they're producing.

But we also developed a couple of very targeted lists of chemicals. And we -- for that, we used EPA proposed test methods under development, you know, to identify the specific substances that they will be asking wastewater managers to report. And so there's a list of

roughly, I want to say, about 170 chemicals that could potentially -- I mean, that are identified individually in our list and that could potentially be having a detection method developed in the near future.

PANEL MEMBER KLEINMAN: Thank you.

CHAIRPERSON ANASTASIO: Okay. Great. Thank you, Mike.

Any other comments?

Okay. So then let's think about moving into part two. So part two, as I mentioned, is going to be the prospective discussion on future updates to Appendix A of the EICG. And they're going to invite discussion of potential future pathways for the Hot Spots Program. And so we'll be talking about, you know, how do we -- how does CARB update the appendix in the future?

So Gabe is going to give his presentation, then the Panel will have a discussion, and then we will open it up to members of the public. So any member of the public who would like to comment, I encourage you to either raise your hand, and then I will call on you or you can submit your written comment in the chat. Please don't do both, because then it gets just more confusing to keep track of all the comments and which ones we've already addressed.

We, as a Panel, and certainly CARB, as an agency, are particularly interested in hearing about potential

ways we might support air quality improvements and health protection at the community level. Okay. So I bring it back to Gabe, who will give us the part two presentation.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Thanks again, Cort. So yeah, in part two of this presentation, we're going to be asking for your recommendations and feedback on the ways that we, you know, could improve the process for updating the chemical list, in particular, when it comes to the engagement of the Scientific Review Panel.

So next slide, please.

--o0o--

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: In order to obtain the program's goal of protecting public health, it is critical to update the chemical list on a regular basis. So to that end, we have developed a plan to update the list on a recurring five-year cycle. And with this plan, we would implement an iterative process in years one to three to identify and evaluate candidate substances in consultation with OEHHA and DPR staff. That's the Department of Pesticide Regulation.

In years three and four, we would engage the Panel to provide state-of-the-science input and recommendations on the proposed list, and we would also begin the public rulemaking process. We have workshops or

other opportunities for public engagements.

On year five, after modifications to the list based on recommendations by the Panel and public input, we would present the final chemical list to our Board for consideration as part of a formal amendment to the EICG regulation.

So with the above five-year plan in mind, we would like to ask the Panel the following questions.

Next slide, please.

--o0o--

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: So the first questions pertain to the timing and the process itself. First question is, does the time frame for engaging the Panel in years three and four of the review cycle seem reasonable?

And the second question is, based on your experience in the last round of updates, should we consider making any modifications to the Panel engagement process?

And, Cort, I don't know if you would like us to initiate the discussion now or would you refer that I go through all the questions and then --

CHAIRPERSON ANASTASIO: I can keep very few things in my mind at once, Gabe, so let's go slide by slide.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Okay.

CHAIRPERSON ANASTASIO: So, Panel members, any input on these questions?

Well, I'll start the discussion. To me, it seems like the time frame for engaging us is good. You know, this essentially means, you know, every four years, we'll see you talking about updates. And I know that it had been quite some time between the previous update and this current update. So I suspect that the next round will be much smaller than what we've seen in this current round. So this kind of time frame seems reasonable to me.

Kathy, your thoughts?

PANEL MEMBER HAMMOND: Yeah. I'm wondering is this an ongoing plan? Is the proposal that it would be -- this would be a five-year cycle that would continue ongoing, so the --

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yes.

PANEL MEMBER HAMMOND: Okay. Great.

And other than that, yeah, I guess -- I guess this does make sense, yeah. I was trying to think whether you should inform us during that first couple of years, but yeah, I think waiting for the third year would be fine.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yes. And also, you know, five year is kind of a, you know, goal, I mean, give or take a year -- give or take a year. So, you know, it could be six years, but we plan to keep this on a pretty tight schedule, if we can. Yeah, what we are trying to avoid is having 800 chemicals to review, you know, the next time around. So hopefully, as Cort said, it will be a much smaller number.

CHAIRPERSON ANASTASIO: Thank you, Gabe.

Panel members, any comments on the second question in terms of should CARB modify how they're engaging with the Panel, getting our input about this process?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: And if I can offer some, you know, I guess, information to jog your memory. When we first presented the list of chemicals to you, you know, we were asked to do it in PDF documents, also to present the full proposed list. You know, so after we got some feedback from, you know, individual members, some people preferred actually to see an Excel version of the -- of the document. And other members asked for a clean copy of the existing version and then modified copy, you know, with the chemical.

So we definitely are able to, and willing to,

provide anything that would make your review easier, you know. So if -- before we even get started on the next round if you let us know whether you have any specific preferences, then we would take that into consideration as we plan our return, you know, to update you on the next proposal.

CHAIRPERSON ANASTASIO: Yeah. Okay. Thanks, Gabe. Yeah. I thought the Excel and the PDF was very helpful. Of course, if moving forward we decided something else might be helpful, we'll let you know.

Mike, you have a comment.

PANEL MEMBER KLEINMAN: Yes. To me, the Excel spreadsheet was the most useful. And highlighting within the Excel spreadsheet, the new additions and maybe a color code for what stage of consideration they're at could be helpful to focus our attention.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Okay.

CHAIRPERSON ANASTASIO: Thank you, Mike.

Kathy.

PANEL MEMBER HAMMOND: I agree with what Mike just said. And in turns out, I agree with someone on the chat, but I had raised my hand ahead of time on this. I think it might be important also to list some sort of prioritization on these lists, so that, you know, whether

it's one, two, three -- you know, categories one, two, and three, or something, because -- and if there are a lot of chemicals, you're not going to be able to do them all simultaneously and make apparent what is the way in which you prioritize, both by degree of exposures, you know, the number of people, the extent of the exposures, and whatever is already known by the toxicity. But, you know, it's not an easy thing to do, but I think it should be transparent how you're prioritizing.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Thank you.

CHAIRPERSON ANASTASIO: So just from my clarification and maybe the rest of the Panel's, so Gabe, you know, CARB makes a list of Appendix A chemicals, but OEHHA decides on the prioritization for health guidance values, is that correct?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yes, that's correct.

CHAIRPERSON ANASTASIO: Okay. Yeah.

Other comments about these two questions?

Yes, go ahead, Paul.

PANEL MEMBER BLANC: So just a follow-up to that last question, you submitted a list of new things to add and you're waiting for CARB to approve that list, do I understand that process part correctly?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: So we updated the list of chemicals that must be reported to CARB. And so we went from roughly 450 that had existed on the list for the last, you know, many -- 15 years maybe. We added over 900 new chemicals, many of them came from lists that we are required to review and then -- you know, there's six lists in statute that we are required to check and those substances that can become airborne to our list of reportable substances.

And then there were maybe another three to four hundred chemicals that we reviewed in consultation with OEHHA and DPR to determine whether -- you know, first of all, can they become airborne, and second do they present some short potential health risk to public health.

So we have this list. It was approved -- the list -- or the updated list was approved by our Board about almost a year ago now. So we have been working on, you know, finishing up the regulatory process. And it's still -- the whole package is now under review by the Office of Administrative Law, which is almost the last step before the regulation amendments become official.

So barring any, you know, last minute issues, which we don't anticipate, the OAL, you know, will approve -- we're hoping they will approve our package. And then it goes to Secretary of State, and then, at that

point, the regulation becomes -- or the amendments become effective.

The second part is OEHHA's role in this. I mean, they played a very, you know, strong support role in helping us identify and -- identify the chemicals that should be added. But for further down the road, they will be developing peer-reviewed health values for some of these chemicals. And this list helps in their prioritization, but it's not a requirement that they take all the chemicals from our list.

PANEL MEMBER BLANC: Right. And that's certainly back to this question of prioritization, because I think from our point of view, perhaps more important than what's on this master list is what is -- what are the priorities for them developing a closer look? And I think it was stated that that's going to be the Air Resources Board that makes -- that drives that prioritization, or will it be OEHHA itself, or -- I'm still not clear on that part. Because to us, that was always -- historically has been the issue, as much as adding new chemicals to the possibility of being prioritized.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yeah, I would say the -- at least, you know, when it comes to the emission inventory that we create, it's -- that is part of the kind of feedback loop. I mean, so it

does inform, to some extent, OEHHA's decision to prioritize certain chemicals, you know. And, I mean, we do have regular conversations with John Budroe about, you know, do we have this chemical in the inventory, what are the emissions that are being reported to us?

But they also look at other data bases, you know, where facilities are required to report to EPA, for instance, PRIs and other source. And I'm sure John can, you know, provide more information on that.

But, yeah, so what we see this as is we create a list of chemicals that we think should be reported, but are not being reported, then we get a sense of, well, how much of it is being used. And then maybe looking at, you know, some of these provisional health values determine how -- what is the potential for some of these chemicals to become a localized health issue. And, you know, something what would inform OEHHA's decision to, okay, we need to develop health values for these particular chemical. So it's all part of a feedback loop, like I said.

DR. BUDROE: Right. And that includes the air districts also, because they have an idea of what their facilities are emitting and they -- and come up with concerns. They get input from their communities and -- you know, that's one of the -- one of the input sources

that we have also.

CHAIRPERSON ANASTASIO: Yeah. Thank you, John. Thank you, Gabe.

Joe, comment?

PANEL MEMBER LANDOLPH: Yeah. I was thinking about this last meeting too and it carried over to this one. It seems to me you almost need some risk assessment calculations, like which chemicals - and I'll focus on carcinogenicity first - have the highest cancer slope factors, and multiply that by the concentration, and see which stick up like the weeds above a lawn, and go after those.

And the same thing with toxicity, use the toxicity slope factor and multiply that by their -- you know, the concentration that you measure, that you can assume is an average concentration and do a screening like that to get the really bad actors out of the pile first would be a suggestion.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yeah. Thanks. So what we're trying to do, and so the reason why we need to update our regulation is, yeah, there's a lot of, you know, emerging or new chemicals, things that were not in use, you know, 20 years ago. So through our contacts with environmental advocates, we've -- environmental scientists, we have -- we

learned -- you know, during our regulatory public process, we learned about chemicals that, you know, should have been added to the list many years ago and we have not done that yet.

So the first bit for us is always -- you know, to determine, well, is this chemical being emitted in California and in what numbers? And then that informs, you know, well, the decision to prioritize a particular chemical -- a particular group of chemicals for further review by OEHHA to determine, you know, what those health risk numbers are.

So we work closely together, but we have to start somewhere. And putting those chemicals on the list that must be reported is the first step. And otherwise, we would be speculating, you know, whether something is being emitted or not in the state. And we could potentially be misusing OEHHA's resources, you know, to the first -- go after something that is not -- that does not represent a risk in the State.

PANEL MEMBER LANDOLPH: Yeah. As long as you're working with OEHHA and to have them do risk assessment calculations, that would be fine. One of the things I hate to see and I think we have to think about it in terms of regulation is, you know, we're getting longer and longer lists of chemicals. And, you know, some of them

fade out, because they don't have a really high slope factor, whether for toxicity or cancer, and the exposure concentrations may be small, given a product, which is small.

So I think it's important that we go after those that are -- you know, have high slope factors say for cancer, for carcinogenesis, and high concentrations, and pull those out of there and focus attention on them, so that we can get the most action per dollar invested and help protect the health of the people.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Thank you. I think that's exactly our aim too. So we concur with your assessment.

CHAIRPERSON ANASTASIO: Yeah. Thank you, Joe.

PANEL MEMBER LANDOLPH: Thank you.

CHAIRPERSON ANASTASIO: Gabe, let's go to the next slide, your second list of questions.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Okay. So next slide, please.

--o0o--

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Some of these questions, you know, we have already touched upon in our first -- in responses to our first question. But yeah, this question is specifically about the identification of emerging chemicals. And so does the

Panel have recommendations on the approach or resources that we should consider when identifying candidate chemicals for addition to the list?

And as I mentioned earlier, you know, during the last panel updates, you pointed us to three very useful resources that were ACGIH -- ACGIH, NIOSH, and the Olson Toxicology Handbook. So we're wondering, you know, if you have any other resources in mind that, you know, off the bat, we should consult when we create the next list of candidate substances?

CHAIRPERSON ANASTASIO: Kathy, go ahead.

PANEL MEMBER HAMMOND: Those sound good. And I couldn't I -- you blocked out for a minute there, but if you said it, my apologies. The REACH list, the European, I mean, I would definitely look -- be monitoring that.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Okay.

CHAIRPERSON ANASTASIO: Joe.

PANEL MEMBER LANDOLPH: Stick with carcinogenesis for a second. You know, for cancer, the cancer slope factors span about a factor of a million. So there are things like tamoxifen, which are reasonably weak. And then there are things like, oh, aflatoxin, for instance, which are incredibly strong. So it might be not that difficult to compile a list of these based on a cancer

slope factor to start out with, you know, to help prioritize these and then later on add the concentration to get the product.

The same thing for toxicity, you could get the things like dioxin, which have really high toxic slope factors, and then other things which are more prosaic and we might not have the time, or the energy, or the resources to regulate, because they're not that big a threat, and just kind of triage some of these things and move the important ones up to the top.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yeah. Thanks. And, in general, you know, when OEHHA has developed cancer factors or other -- or RELs, we tend to look at those first. You know, so many of these substances have been in our list for a long time. So mainly what we are doing with now and in the near future will be emerging chemicals, I mean, things that we had not thought about yet.

You know, so this is all kind of going to be kind of out there, you know, kind of pushing the envelope of new chemicals that maybe should be added to the list.

CHAIRPERSON ANASTASIO: Okay. Thank you, Joe.

Paul.

PANEL MEMBER BLANC: Just remind us is this -- the list -- when you add new things, does it exclude or

not exclude agricultural chemicals?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: It does not exclude agricultural chemicals. So, for instance, if -- during production of pesticides, there are emissions at the facility, then those have to be reported. If after the use of a pesticide, there are emissions such as fumigation, you know, at a facility, when the fumigant is being vented to ambient air, then those are included in the -- in the list of activities that must be reported.

It's only when they are being used for their pesticidal use, you know, that they are excluded. So there is an exclusion in the statute that essentially --

PANEL MEMBER BLANC: Function --

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: -- agricultural products being used, you know, for their agricultural intended use are not part of this program.

PANEL MEMBER BLANC: So I think that one challenge with the sources that we had recommended and then you were using before going ahead with adding on additional chemicals that are associated with emerging technologies and emerging industries is that the -- is the -- you know, the lag time before there's enough recognition or attention to them to filter down to some of

those lists. So you may want to consider an industry-specific strategy where you select certain high-impact industries that can be characterized by a lot of introduction of -- or potential introduction of new chemical materials.

So an example would be the battery industry as just one example, and I would say, you know, display terminals, and micro-electronics, and, you know, just a handful of industries that -- and -- you know, and also the urethane related things, where I'm not exactly sure what the best sources would be to catch these substances, other than trade journals where they tend to be talked about a bit.

So I don't have a simple fix, but if the emphasis is on emerging or industries that tend to be characterized by emerging new chemical moieties, then you should probably take an industry-specific choice. That's why I asked about ag chemicals, because things like herbicides that are being introduced with regularity, and flame retardants, and, you know, modifications of existing things are one approach, I suppose.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yeah. So we do consult with Department of Pesticide Regulation staff as we do our updates to the list. But, yeah, that's a very good point. Thank you.

CHAIRPERSON ANASTASIO: Thank you, Paul.

You know, Gabe, on that note, I imagine you guys do annual literature searches through PubMed or other science to try to -- you know, searching for emerging contaminants or emerging air toxics. That's going to be probably faster turnaround than some of the handbooks.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yeah, I think, one of the things -- that's definitely one of the things that we need to do. This time around we were being a little bit more reactive. I mean, so when we start working on the regulation, you know, we still -- it took us a while to figure out what the scope of the amendments needed to be.

Then by the time we kind of settled down on exactly how much we wanted to do, basically we just decided to play catch-up at that point. But I think going forward, yeah, taking a more proactive approach will be useful in, you know, keeping us up to date on what's going on out there.

CHAIRPERSON ANASTASIO: Yes, Mike.

PANEL MEMBER KLEINMAN: Yes. The -- some of the emerging industries, you know, as our technology, you know, changes, provide a lot of possibilities. For example, recycling of lithium batteries with our move to an electronic -- you know, electric vehicle

infrastructure, and more and more electric cars, et cetera. Recycling these newer batteries is going to lead to a lot of emissions of things that are not governed.

And I was noticing on -- in Appendix A, at least in Table A1, lithium wasn't listed. And lithium does have some toxicity and may become, you know, important in the future.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Okay. Thanks. We will like into that.

CHAIRPERSON ANASTASIO: Great.

Gabe, how about we move to the next slide. I believe you have five total questions?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Actually, there are only three questions, you know. So as we were --

CHAIRPERSON ANASTASIO: Oh, okay.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: -- working on our presentation, we condensed a couple of them into one, but, yeah.

CHAIRPERSON ANASTASIO: Okay. So this is the last slide?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yes.

CHAIRPERSON ANASTASIO: Okay.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER

RUIZ: Last question is -- so we added three functional groups PAHs, isocyanates, and halogenated PAHs. So the is does the panel have recommendations on other classes of functional groups that we should consider for addition in the next round of updates?

CHAIRPERSON ANASTASIO: I know we had given several suggestions for functional groups, some of which you adopted, some of which weren't feasible. But let's open it up again. So, Mike, thoughts?

PANEL MEMBER KLEINMAN: Yeah. This is not really -- well, it's kind of a functional group, but going back to the PFAS, PFOS, PFOA type compounds. They're all part of a huge family. But looking at the toxicology data that's emerging, it seems like the compounds in the range of seven carbons in the backbone up to, I think, eight or -- eight or nine tend to have the greatest amount of toxicity. And so there may be ways to group families of compounds by structure activity relationships. And that may be a way to deal with some of these things, where, for example, as you regulate one of the PFAS compounds, they add something to it and change it moderately. But it's -- you know, it has the same say fire retardant capability, but it's no longer exactly the same as it was. So some structure activity relationships might be helpful.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER

RUIZ: Okay. Thank you.

CHAIRPERSON ANASTASIO: Thank you, Mike.

Any panel member have recommendations on another functional group classes?

I mean, Gabe -- I guess maybe this is a question for OEHHA, but, I mean, working out, how do you regulate a class is still a topic of a discussion, right, how that -- how that's going to look?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yes. Yes. So the function -- or, you know, the role of the Hot Spots Regulation is only to gather information of what is being emitted. So when it comes to additional regulation of specific substances, I mean, that's outside the scope of the AB 2588 program that we oversee. So, yeah, it would be up to -- you know, I mean, potentially one of our sister divisions that CARB might be coming up with ATCM, Air Toxic Control Measures. I mean, if we determine that, you know, there's some need to control a specific substance. But again, all of that is done really outside the scope of the EICG.

CHAIRPERSON ANASTASIO: Yes, I see. Thank you.

Anything else from the Panel about functional groups?

Karen.

PANEL MEMBER MESSER: Yeah. This is a little bit

outside my area of expertise, but just wanted to mention there are these chemometric -- following up on one of the prior comments from one of our panelists, that there are these chemometric classifiers that can classify chemical compounds. And those can be very useful, for example, in high throughput screening studies that I've participated in, like Merco classes or Tanimoto clusters. So just following up on that idea as a way of grouping these compounds that might help to prioritize classes of compounds.

CHAIRPERSON ANASTASIO: Yeah. Okay. Thank you.

Any other Panel comments on either this question or any of the other questions that Gabe has raised?

So I have one comment. I mean, we talk about prioritization and that's definitely important, but I've said this before, but I think it's an important point, so I want to say it again, you know, if we look at the 900 new chemicals added to Appendix A, we can do -- we and OEHHA do roughly two to three chemicals a year.

So I don't think I'm going to make it for the whole list. So this idea of provisional health values is hugely important. And I think part of that -- you know, I wonder how much of setting values is going to be limited by the current requirement for animal or human data. And so I hope that within the provisional health values in

vitro assays can be used to come up with some initial estimate of whether something is high, medium, low toxicity.

And, John, I don't know, I know John Faust talked to us about provisional health values a year or so ago, but can we look forward to an update on the progress there?

DR. BUDROE: I'm hesitant to speak for another branch, as far as how they're going on that, but --

CHAIRPERSON ANASTASIO: Okay

DR. BUDROE: -- I mean the SNAPS Program, which is a oil and gas production monitoring study and risk assessment in communities near those facilities. They are essentially looking at surrogate values for risk assessment health guidance values. And some of them are, for example, using values from other programs and either U.S. EPA or other states. So that's progressing.

And there's a -- they're trying to work in things likes read-across as much as possible, but they're working with a lot smaller analyte list also. I mean, they're working with essentially VOCs that are detected near those communities. So the size of the list is a lot smaller than what is going to be going into the Appendix A list.

CHAIRPERSON ANASTASIO: Okay.

Yeah. I mean, we've got to figure out a way to

increase the throughput on at least rough health guidance values to have any chance of getting through this list.

Any other Panel comments?

Okay. So then what I'd like to do is I'm going to open it up to public comment. So if you would like to comment -- oh, sorry, Gabe, were you not done?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Oh, yeah. Well, I have just one final slide talk about --

CHAIRPERSON ANASTASIO: Sorry. Yes, go ahead.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Okay. Thank you. So we can go back to the next steps slide. There you go.

So as I mentioned, the regulatory package is being reviewed by the Office of Administrative Law. And we anticipate that the adopted amendments will become effective early next year. In the interim, we will be working on developing guidance material to assist facilities and air districts with implementation of the revised -- or of the amendments. We anticipate that we will get started on the five-year review and update cycle for chemicals -- for the chemicals list next year. And also make sure we will continue our discussions with OEHHA and the panel on provisional health values outside of the AB 2588 regulatory framework.

Yeah, next slide.

--o0o--

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: So that ends my presentation. This final slide provides updated contact information, in case anyone would like to follow up with further questions. So I really would like to thank you, Cort, and the Panel for all your value input through the review process. And we look toward to future discussions on this subject.

Thanks.

CHAIRPERSON ANASTASIO: Great. Thanks very much, Gabe. Appreciate your presentation today and all the work you've done to update Appendix A.

So now I'd like to open it up to public comment. So two ways to do this. I see that a number of people have already said something in chat. So I will read those. The other thing you can do is raise your hand. And then I'll call on you and you give your comment verbally. We will have a two-minute time limit on your comment, so try to be concise.

So I'm going to start by reading some of the comments in chat.

So Janet Whittick wrote that this is an issue of prioritization. So the question is, you know, what's the plan for how to prioritize technical evaluations for the

already listed chemicals. And we discussed this several times. So I'm just going to say that this is certainly something that CARB, and OEHHA, and the Panel are all aware of, that we really need to hit the most important chemicals first.

Moira Sullivan had a comment that maybe exposure data should drive the prioritization process, and that certainly PFAS is Significant in that regard. And, you know, Joe had mentioned definitely as part of the prioritization that exposure is going to be an important component

Michael Miller writes that -- let's see this is related to the emission factors for chemicals already on the lists. Any ongoing reviews or plans to review/redo or address the allowed emissions factors from relevancy and/or accuracy. Many of the available emissions factors were derive from limited source test data from the 70s and 80s when methods were in development and analytical instruments had poor detection limits. So in many cases, he believes the emissions factors were set based on those high detection limits and that can be issue when you have a lot of non-detects.

So maybe Gabe send this to you. I mean, my understanding is the emissions data is not typically that old. But can you talk to this issue of emissions factors?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yes. I mean, I think I'll take a stab at it. So we have -- I mean, we have to rely on emissions data that is available. A lot of the methodologies, a lot of the -- yeah, methods for estimating -- these emissions factors, sorry, actually are set by air districts. I mean, so between air districts and us to, a lesser extent, we do search, you know, the literature for the best available data. But, I mean, we're talking about, for instance, different processes, different materials, being used. So it's really hard to, you know, always have like cutting edge -- cutting edge studies on everything.

So the districts and us do our best to keep up with the permission that is out there. But the EICG actually does allow facilities to do source testing. I mean, so they're not -- there's a specific number of facilities that have to do source testing. But districts have the authority to, you know, implement more stringent requirements. And facilities can work with the district to do their own testing, you know, but they have to show essentially that their test is comparable, you know, to whatever emission -- what study was used to derive these emission factors.

So there's nothing precluding anyone from doing some testing that actually shows their emissions are

different from what the -- from what is published in those emission factors.

CHAIRPERSON ANASTASIO: I see. And so these emission factors are then used to estimate risks to the local population, based on the health guidance values?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yes. Yes. That would be the process, so a facility develops an emission inventory. The district does an analysis of the emissions reported and then determines whether the facility has high enough emissions -- you know, a specific -- or chemicals that might drive the risk. And then they determine whether they need to move on into the next phase. So that's called the prioritization step.

And then the next step, these facilities that have a high prioritization score will have to actually conduct a health risk assessment, and a lot of times, the health risk assessment and prioritization scores. You know, the health risk assessment actually they look at very specific parameters, such as where are the emissions actually taking place, how far is the nearest receptor, what is the actual meteorology that impacts the emissions, you know, throughout the entire year.

Sometimes the HRA actually comes down or comes that way if, you know, the risks are not as high as, you

know, potent -- as they could potentially be if the conditions were different.

CHAIRPERSON ANASTASIO: I see. Okay. Thank you.

So Michael Miller who has this question I see he's actually online. Michael, can you -- do you want to clarify your comment or follow up?

MR. MILLER: All right. Can you -- can you hear me now?

CHAIRPERSON ANASTASIO: Yes.

MR. MILLER: Hello?

CHAIRPERSON ANASTASIO: Yes. Can you hear me?

MR. MILLER: It looks like I'm having some issues with the audio.

CHAIRPERSON ANASTASIO: Oh, shoot. Okay. Okay. You can't hear me. Michael, I will move on to the next comment and hopefully you can get your audio --

MR. MILLER: I can't speak, so I'm just going to get off the mic here.

Can you hear me now?

CHAIRPERSON ANASTASIO: Yes. Can you hear me?

MR. MILLER: All right. So the question I had actually goes with that -- the actual, you know, requiring of the sources. So when we go through the risk assessment, we were given a bunch of different factors like, you know, Long Beach factors AP-42. In many cases,

when you plug those factors into the risk assessment score, you get these arbitrarily high values, which it actually forces the source into doing a test. In the case of diesel fuel out of combustion source, the test is in the neighborhood of like 50,000 to have a tester come out and test for all the compounds.

And then when we went and researched these factors and found out that the factor was based off of, like I said, source test data from the 70s very limited, and it was a non-detect. And so it was an arbitrarily high value. And so it really screwed -- rather skewed the risk assessment really high. And it kind of forces every source in that category to do a source test. And so it would be very helpful, at some point, to start going through the -- maybe with the air boards and gather data on sources that did a source test in lieu of a using a factor. And then to look at those factors and maybe put some resources towards developing more modern or, you know, say better factors that categorize the -- what's actually coming out.

Since there is a lot of source test data right there. With the sources, you guys will have actually some pretty good source test data to use and that's my comment.

CHAIRPERSON ANASTASIO: Thank you, Michael.

Gabe, any response?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yeah. I mean, I think it's something that we definitely need to take offline. We do plan, you know, as part of the implementation of the amendments to the EICG and companion regulation, which is the criteria and toxics reporting reg, we do plan to, you know, have a number of working groups with local air districts through the California Association of -- California Air Pollution Control Officers Association, or CAPCOA. So I think that's probably a much better forum, you know, to bring up these issues.

Yeah, I think this is way too detailed and I don't have all the technical expertise that it would require to answer those questions. A lot of this work is really done by the air districts. And so we do work with them, you know, very closely, but it involves a lot of people with very specific technical expertise.

CHAIRPERSON ANASTASIO: I see. Thank you, Gabe. And thank you, Michael, for the comment.

The last comment I see is from Rita Loof. And Gabe, this is a question for you again. Is the list of 110 compounds that was mentioned in addition to the 900 compounds currently included in appendix A?

So I think maybe the question is can you go over the numbers again in terms of number of species that were

already in Appendix A and then the new ones you added?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yeah. So there were 450 chemicals roughly in the chemical list as it existed before the amendments. We added over 900 -- close to 1,000 new chemicals to Appendix A1 and that does include the 110 chemicals that I mentioned. So it includes all of the ACGIH chemicals, the NIOSH chemicals, PFAS. Everything that I mentioned during the presentation, that's part of the nearly 1,000 chemicals that we added or the 900 plus chemicals that we added.

CHAIRPERSON ANASTASIO: Thank you, Gabe.

So I just have a follow-up question. Of the 450 in the previous Appendix A list, do you know how many of those have health guidance values roughly?

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: I just looked at that number. I'm sure it's -- I mean, it's a fraction, but it's close to half. I want to say --

CHAIRPERSON ANASTASIO: Close to half. Okay.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: -- maybe about -- I mean, don't quote me, but I seem to recall like roughly 170 or so, but I would have to go back and check. But it's a pretty significant number. But then when you look at the total number in the new

list, then it becomes a much smaller fraction.

CHAIRPERSON ANASTASIO: Yeah. So that's interesting, right. So you're talking -- if you've got 170 health guidance values out of roughly now 12 -- 1,300 chemicals that we're talking, you know, 10, 15 percent of the species actually have health values.

AQPSD TOXICS INVENTORY & SPECIAL PROJECTS MANAGER RUIZ: Yeah. It's a very -- relatively a very small number altogether.

CHAIRPERSON ANASTASIO: Yeah. Any other comments from the Panel about our Appendix A discussion?

Okay. Seeing none. I'd like to thank Gabe for his presentation and all the work that he and CARB have done on updating the EICG.

The last topic on our agenda for today is administrative matters. First, I'd like to remind the Panel to make sure it's in your calendar. Our next meeting will be Thursday, May 12th, starting at 9:30. We'll probably run till 2:30, so we'll take a break for lunch on that day.

Also, Daryn reminded me through the chat that I really forgot to dispose of the 1-bromopropane discussion in terms of your next steps. So I would propose that since there were pretty minor comments overall that aren't going to affect the IUR that Daryn revises the document,

sends it to me with a CC to Ahmad and Karen, and then I'll look it over. And Ahmad and Karen, if you have any comments on that, then you can let me know and then I'll just tell Daryn otherwise that it looks good or not. And I am sure it will look good at that point. So and that's how we'll proceed on that.

The last topic is that I'm not sure if everybody knows this already, but today is Lori Miyasato's last day at CARB, and therefore with the SRP. So I wanted to thank you Lori for all of her help over the last two years and just say a little bit of information I got about Lori's service at CARB from her manager Hye-Youn park. So Lori has worked at CARB in the Research Division for almost 19 years and then that includes the last two years with Liaison to SRP. She's been a staff lead for multiple important projects, such as the NAAQS review, neurotoxicity study, and ultra fine particle health research. She was also a lead staff to quantify health impacts of CARB regulations, such as the Carl Moyer Rule.

She's managed more than 16 research contracts, including wildfire smoke exposure in infant Macaques and immune respiratory impacts. That sounds like Lisa Miller to me. I don't know.

As a recognition of her hard work and dedication, she received three CARB Gold and Silver Superior

Accomplishment Awards. She also gave multiple Board presentations on neurotoxicity, and air pollution, and childhood respiratory allergies. She's a great scientist with excellent organizational skills and subject matter expertise. And she is also a genuinely nice person to work with that everyone at CARB and on the Panel will miss.

So Lori, thank you very much for your many years of service to CARB and to the SRP. We're sorry you're leaving us, but we're happy that you're really just moving next door to OEHHA, so we can take some solace in that.

You can now have a rebuttal Lori, if you'd like.

PANEL LIAISON MIYASATO: Thank you very much, Dr. Anastasio. It has been an honor to work with this Panel. It's only been two short years, but this has been a great experience and I've learned so much from you all, as well as from the program staff at OEHHA, and CARB, and DPR. It's really great to see the scientific review process in action. And it kind of restores my faith in science, if it has ever been off. So I just wanted to thank you. I think you're all great. You're all models. And this will help me as I move on in my career.

This has been one of my most rewarding assignments in my time at CARB. And so I really appreciate everything that you all do.

Thank you so much.

CHAIRPERSON ANASTASIO: That's great. Well, thank you, Lori.

It looks like Mike would like to say something.

PANEL MEMBER KLEINMAN: Yeah, I just wanted to add to what you just said. I've worked with Lori as a program manager. She managed some of my research over the years and has always been a remarkably helpful and thoughtful person to work with. Also she's had remarkably good insights into science and the application of neurotox to the kinds of studies that we've been doing. And she's often, you know, added a lot of value to the research project or products that we've generated over the years. So I wanted to thank you for that as well. And I'm really happy that you're staying engaged. And I think you deserve to have a wonderful experience in your new job.

And thank you.

PANEL LIAISON MIYASATO: Thank you so much, Dr. Kleinman. It's been great working with you. And I'm kind of sad to have to give up these contract projects that I've worked with you on. Thank you.

CHAIRPERSON ANASTASIO: Great. Thank you, Mike.

All right. Well, anyone else want to say anything about anything?

Okay. I'm then looking for a motion to adjourn.

PANEL MEMBER KLEINMAN: So moved.

PANEL MEMBER HAMMOND: Second.

CHAIRPERSON ANASTASIO: Thank you very much. I'm now looking for a vote on adjournment.

All in favor, you just raise your physical hand.

(Hands raised.)

CHAIRPERSON ANASTASIO: All right. We are unanimously done. Well, thank you very much everybody for your attendance today and your input. Appreciate that. Thank you to OEHHA and CARB staff for their presentations. And we will see you in May. And who knows, maybe it will actually be in person. We'll see how that goes.

All right. Have a good weekend, everyone.

(Thereupon the California Air Resources Board, Scientific Review Panel adjourned at 12:43 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 Air Resources Board, Scientific Review Panel meeting was reported in shorthand by me, James F. Peters, a Certified Shorthand Reporter of the State of California;

That the said proceedings was taken before me, in shorthand writing, and was 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 25th day of October, 2020.

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