MEETING

STATE OF CALIFORNIA

ENVIRONMENTAL PROTECTION AGENCY

AIR RESOURCES BOARD

SCIENTIFIC REVIEW PANEL

ON TOXIC AIR CONTAMINANTS

ZOOM PLATFORM

CALEPA HEADQUARTERS

1001 I STREET

SIERRA HEARING ROOM

SACRAMENTO, CALIFORNIA

FRIDAY, FEBRUARY 2, 2024

9:30 A.M.

JAMES F. PETERS, CSR
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APPEARANCES

PANEL MEMBERS:

Cort Anastasio, PhD, Chairperson

Ahmad Besaratinia, PhD

S. Katharine Hammond, PhD

Joseph R. Landolph, Jr., PhD

Pamela Lein, PhD

Karen Messer, PhD

Beate R. Ritz, MD, PhD, MPH

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Brian Moore, PhD, Manager, Community Planning Section, Community Planning Branch, Office of Community Air Protection

REPRESENTING THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT:

Kannan Krishnan, PhD, Chief, Senior Toxicologist, Air and Site Assessment and Climate Indicators Branch, Division of Scientific Programs

Rona Silva, PhD, Staff Toxicologist, Air Toxicology and Risk Assessment Section, Air and Site Assessment and Climate Indicators Branch, Division of Scientific Programs

Craig Steinmaus, MD, MPH, Pubic Health Medical Officer III, Water Toxicology Section, Pesticide and Environmental Toxicology Branch, Division of Scientific Programs

Rima Woods, PhD, Chief, Air Toxicology and Risk Assessment Section, Air and Site Assessment and Climate Indicators Branch, Division of Scientific Programs

APPEARANCES CONTINUED

ALSO PRESENT:

Claire Conlon, Biocom California

The Original Dra

Lucy Fraiser, PhD

Keya Gupta

Kathy Kerridge

Alex Khan, California Chronic Care Coalition

Abby Li, PhD, Exponent

Aracely Campa Ramirez, California Life Sciences

William Remak, California Hepatitis C Task Force

Richard Reiss, ScD, Ethylene Oxide Sterilization Association

Jane Teta, DrPH

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PROCEEDINGS

CHAIRPERSON ANASTASIO: So I'd like to call the meeting to order. I'd like to Welcome everyone to the meeting today and remind you that it is being recorded. Arash is going to be overseeing the Zoom technical operations and he's going to give us instructions or give the public instructions later for how to comment. Panel members, when you want to comment, if you could raise your hand in Zoom. That's going to be the most efficient way.

Okay. So I'm going to introduce the panel now. Before we go around the room, just a couple notes. So Kathy Hammond, and Mike Kleinman, and Paul Blanc are all rotating off the Panel this year, so a big change for us. I'd like to thank all three of them for their service. And I'm happy to say that Kathy and Mike are going to join us this morning. Paul cannot.

Let's go around the room then and have introductions of the remaining panel. I will start. I'm Cort Anastasio. I'm Chair of the Panel and I'm a professor at UC Davis.

Karen.

PANEL MEMBER MESSER: Thank you, Cort. I'm Karen Messer. I'm a professor of biostatistics at University of California, San Diego, and I'm the Director of Biostatistics at the Moores Cancer Center.

CHAIRPERSON ANASTASIO: Thank you, Karen.

Pamela.

PANEL MEMBER LEIN: Good morning. I'm Pam Lein. I'm a professor of neurotoxicology in the School of Veterinary Medicine at University of California, Davis. And I'm also Chair of the Department of Molecular Biosciences there.

CHAIRPERSON ANASTASIO: Thank you, Pam.

Ahmad.

PANEL MEMBER BESARATINIA: Good morning, everybody. I'm Ahmad Besaratinia. I'm a professor of population and public health sciences at University of Southern California here in Los Angeles.

CHAIRPERSON ANASTASIO: Thank you, Ahmad.

Beate.

PANEL MEMBER RITZ: Yeah. I'm Beate Ritz. I'm a professor of epidemiology and environmental health as well as neurology at UCLA. Former Chair of Epidemiology at UCLA and a member of the Center for Occupational and Environmental Health in Los Angeles.

CHAIRPERSON ANASTASIO: Thank you, Beate.

And Joe.

PANEL MEMBER LANDOLPH: Hi. I'm Joe Landolph, I'm associate professor of molecular immunology, molecular microbiology, and immunology, and pathology and a member

of the USC Norris Comprehensive Cancer Center at the University of Southern California.

CHAIRPERSON ANASTASIO: Great. Thank you very much, Joe. As I mentioned earlier, I do expect Kathy and Mike to join us, but they're not here yet, but we have a quorum, so we'll get started.

Two items to discuss today. The first is from OEHHA. It's kind of an intermediate stage of cancer assessment for ethylene oxide, EtO. And then after that, we will have an item from OCAP, an informational update on the Community Air Protection Program.

I'd like to remind the public that we're going to be accepting oral comments on both of these items. Arash is going to post the link to the portal in chat and show it on the screen at the end of each item when it's time to have public comment. And if anyone is in person at CalEPA, they need to sign their name on the sheet. And those who want to provide comments virtually, will have to raise their hand once we get to that. Arash is going to show the instructions before we get to or at the beginning of the public comment period. So we won't see that now, but we'll see it later.

Okay. So our first item is an informational item from OEHHA on the scientific issues and the cancer risk assessment for ethylene oxide. OEHHA released the draft

updated cancer inhalation unit risk factor, or IUR, for ethylene oxide for public review on April 7th, 2023. The public review draft document can be found on the OEHHA webpage. The draft was made available for public review and comments until June 14th of 2023. And then OEHHA also held two public workshops on May 5th and 16th in 2023.

Today, OEHHA staff are going to make a presentation on the public review draft for the ethylene oxide IUR. They're going to discuss some of the issues that were raised in public comments and they're going to discuss their draft approach for the revision.

The Panel is going to give feedback on the key scientific issues and input to OEHHA for moving forward with this assessment. So this is not our typical IUR. This is not the finalized version. This is an interim version that we're going to give them feedback on the directions and things that they might want to consider. And then they'll make a complete version that we will then consider at our next meeting. So OEHHA is going to revise this document based on our big picture comments and they're going revisit the IUR next meeting.

So I would allow -- now like to introduce Dr. Kannan Krishnan, Chief of the Air and Site Assessment and Climate Indicators Branch of OEHHA.

Dr. Krishnan.

(Thereupon a slide presentation).

DR. KRISHNAN: Thank you. Good morning, all. I'm Kannan Krishnan, Chief of the Air and Site Assessment and Climate Indicators Branch. And we'll be making this presentation along with Dr. Rima Woods, Chief of the Air Toxicology and Risk Assessment Section at OEHHA.

With us here today are two members of the OEHHA team that contributed to this draft. Dr. Rona Silva, staff toxicologist in the Air Toxicology and Risk Assessment Section and Dr. Steinmaus, a public health and medical officer at OEHHA.

Additional OEHHA authors and reviewers of the draft are here in the room or online via Zoom.

[SLIDE CHANGE]

DR. KRISHNAN: At the outset, I would like to go over briefly our process for developing a health guidance value under the Hot Spots Program with specific reference to the inhalation unit risk factor, or IUR, for ethylene oxide. OEHHA released a public review draft in April 2023 and we have received public input through oral and written comments.

During the public comment period two workshops were held, one in Northern and one in Southern California. That's the second box here in this figure. And today, we will be presenting -- as the Chair already indicated,

we'll be presenting the public review draft to SRP for your input. And we will also give you an overview of some of the issues raised in the public comments that we received thus far on the draft. So we're at the third box in this slide.

The next three boxes in this slide capture the remaining steps leading to the adoption of the IUR for ethylene oxide: the revision of the current draft and detailed response to all comments received; then SRP review; followed by further revision of the draft based on a SRP review and adoption of the IUR for use in the Hot Spots Program.

For today, we're looking for the Panel's general input on the development of IUR for ethylene oxide, and specific input about our considerations and the directions we propose to take in addressing some of the issues raised during the public comments.

[SLIDE CHANGE]

DR. KRISHNAN: So just to recapitulate the timelines. The draft updated IUR for ethylene oxide was released on April 7th, 2023 commencing the public comment period, which ended on June 14th. Two public workshops should be -- I mentioned previously were held on May 5th and May 16th. And OEHHA is considering the public comments received thus far.

[SLIDE CHANGE]

DR. KRISHNAN: And here is the outline of the presentation with a tag team approach essentially. So first Dr. Rima Woods will start by providing an overview of how the IURs, or the inhalation unit risk factors, are used in the Hot Spots Program and then present a summary of the updated IUR public comment draft for ethylene oxide. After that, we will pause for any clarifying questions and initial comments from the Panel.

I will then follow by presenting the topics and some of the scientific issues raised in the public comments and discuss OEHHA's thinking regarding these issues. I will conclude by referring to the next steps in the process and then turn it over to the Panel for discussion and input to help move forward with this assessment.

With those initial comments, now I turn it over to Dr. Woods.

[SLIDE CHANGE]

DR. WOODS: Thank you, Dr. Krishnan.

So OEHHA is tasked with developing health guidance values for toxic chemicals that are placed on the Hot Spots list. We developed these health guidance values based on the best available science. And in accordance with our Hot Spots technical support documents. The

health guidance values are used to estimate risk due to emissions from stationary sources. Inhalation unit risks values are calculated for carcinogens and are used to estimate the cancer risk associated with lifetime continuous exposure to 1 microgram per cubic meter of air resulting from a facility's emissions. Once an IUR is adopted, it's used by local air districts within California to prioritize and assess a facility's risk to the surrounding area.

In other words, IURs are applied to exogenous anthropogenic exposures to a chemical that result from a facility's emissions and add to the existing background level.

[SLIDE CHANGE]

DR. WOODS: The draft document that we're discussing today is an update to the previous IUR value for ethylene oxide. OEHHA developed the ethylene oxide IUR in 1987 under the Toxic Air Contaminant Program, when we were part of the California Department of Health Services. That value was based on mononuclear cell leukemia in female rats.

Since then, new research has been published regarding the carcinogenicity of Ethylene oxide. And while no new cancer studies in animal models have been released since our 1987 assessment, several

epidemiological studies have been published. In 2016, U.S. EPA released an updated cancer IUR value for ethylene oxide, based on one of these epidemiological studies.

[SLIDE CHANGE]

DR. WOODS: OEHHA chose to update the ethylene oxide IUR by leveraging the work already completed by U.S. EPA and other health agencies. This approach was presented to the Scientific Review Panel during their May 2022 meeting. The 2016 U.S. EPA assessment exhaustively reviewed the available literature since 1987 and OEHHA used that as a starting point for our update.

We performed a focused systematic literature search to identify studies cited in U.S. EPA's assessment, cited by other authoritative sources, or published since U.S. EPA's 2016 assessment. We thoroughly evaluated U.S. EPA's approach, models, and endpoints during our assessment, all of which I will cover in the upcoming slides.

[SLIDE CHANGE]

DR. WOODS: Ethylene oxide has several uses, and in California it’s mainly used to sterilize medical and lab equipment, and to fumigate agricultural products like herbs and spices. There are at least 34 permitted facilities that emit ethylene oxide throughout the state. Ethylene oxide emissions in pounds are reportable to the

California Air Resources Board under the Hot Spots Program, and at the national level through U.S. EPA's Toxic Release Inventory Program.

In the South Coast Air Basin, background concentrations range from 0.02 to 0.17 parts per billion based on data from 2022 to 2023, and localized monitoring near two medical sterilizer facilities showed levels ranging from undetectable to as high as 103 and 139 parts per billion by volume. Ethylene oxide is found in ambient air and the main sources is an active area of research. Other sources of ethylene oxide include cigarette smoke and release from consumer products.

[SLIDE CHANGE]

DR. WOODS: Ethylene oxide is well established as a carcinogen. OEHHA's predecessor, the California Department of Health Services, listed ethylene oxide as a Proposition 65 carcinogen in 1987. Ethylene oxide was classified as carcinogenic to humans in 2012 by the International Agency for Research on Cancer, or IARC, and in 2016 by U.S. EPA. Then in 2021, the National Toxicology Program classified it as known to be a human carcinogen.

[SLIDE CHANGE]

DR. WOODS: Ethylene oxide is produced endogenously through ethylene metabolism in humans and

other mammals. Ethylene production within living organisms occurs via enzyme-, or copper-, or iron-catalyzed oxidative destruction of methionine, or oxidation of hemoglobin. It also results from lipid peroxidation of fatty acids and metabolic activity of intestinal bacteria. These pathways are well characterized and known to contribute to ethylene production in the body.

I apologize. Let me back up on that one.

Let's go back and talk about toxicokinetics first.

[SLIDE CHANGE]

DR. WOODS: The absorption, distribution, metabolism, and elimination, more broadly known as the toxicokinetics of ethylene oxide have been well studied for ethylene oxide and reviewed in the U.S. EPA 2016 assessment and by the Agency for Toxic Substances and Disease Registry, or ATSDR, in 2022. There are pharmacokinetic models available, which incorporate these toxicokinetic data and show that internal blood concentrations in humans and animals are comparable when exposure to ethylene oxide is less than 100 parts per million. Within this zero to 100 parts per million range, blood concentration has a linear relationship with the inhaled concentration. Ethylene oxide is readily absorbed

through the respiratory tract, mainly due to it's solubility in blood. It's distributed rapidly throughout the body and can bind to proteins such as hemoglobin and to DNA.

There are two major metabolic pathways for detoxification of ethylene oxide. The first is via hydrolysis, which leads to the formation of ethylene glycol and accounts for up to 80 percent of metabolism in humans, compared to 40 percent and 20 percent in rats and mice, respectively. The second metabolic pathway, glutathione conjugation, is the primary detoxification mechanism in rodents.

Radioactivity studies have shown that elimination occurs primarily through urine and exhaled air, with 59 percent of elimination via urine and 13 percent via exhaled air. The half-life in blood is approximately 40 minutes in human, 10 to 19 minutes in rats, and nine minutes in mice. Overall, elimination is faster in rats and mice compared to humans at exposures less than or equal to 100 parts per million.

[SLIDE CHANGE]

DR. WOODS: Okay. And now onto the endogenous production. So as I mentioned earlier, ethylene oxide is produced endogenously results from lipid peroxidation of fatty acids, metabolic activity of intestinal bacteria.

And so these pathways are well characterized and known to contribute to ethylene production in the body. Thus, all species and individuals are likely to be exposed to ethylene oxide endogenously, irrespective of their exogenous exposures to ethylene oxide in the air. The percentage of ethylene converted to ethylene oxide for endogenous sources is unknown, but about three percent of exogenous ethylene is converted to ethylene oxide.

[SLIDE CHANGE]

DR. WOODS: Genotoxicity studies of ethylene oxide have been extensively reviewed by OEHHA, U.S. EPA, IARC, and ATSDR. These studies were conducted in both in vitro and in vivo systems, with and without metabolic activation, and some were observational studies in exposed workers.

In U.S. EPA's 2016 report, they summarized numerous papers investigating the genotoxicity of ethylene oxide and concluded that there is clear evidence that ethylene oxide is genotoxic and sufficient weight of evidence to support a mutagenic mode of action for ethylene oxide carcinogenicity.

In IARC's most recent monograph from 2012, they state, "There is strong evidence that the carcinogenicity of ethylene oxide, a direct-acting alkylating agent, operates by a genotoxic mechanism and ethylene oxide

consistently acts as a mutagen and clastogen at all phylogenetic levels, it induces heritable translocations in the germ cells of exposed rodents, and a dose-related increase in the frequency of sister chromatid exchange, chromosomal aberrations, and micronucleus formation in the lymphocytes of exposed workers."

ATSDR's 2022 toxicological profile reiterated findings from U.S. EPA and IARC, concluding ethylene oxide has been demonstrated to be genotoxic in human and animal studies in vivo and in a wide variety of test systems in vitro. They also discussed the mutagenicity and clastogenicity of ethylene oxide in vitro and in vivo and its formation of nucleic acid and hemoglobin adducts.

OEHHA identified three genotoxicity studies published since US EPA's 2016 review, with two studies in humans and one in mice. The findings from these additional studies are consistent with the overall evidence for the genotoxicity of ethylene oxide.

[SLIDE CHANGE]

DR. WOODS: For the update to the cancer IUR for ethylene oxide, OEHHA reviewed and adapted US EPA's quantitative cancer risk assessment. This assessment used a human epidemiological study, which is preferable to an animal study in that it is more relevant and does not require interspecies extrapolation. Of the

epidemiological studies reviewed by US EPA in their 2016 assessment, OEHHA agrees that the National Institute for Occupational Safety and Health or NIOSH study published by Steenland and colleagues in 2003 and 2004 is the best available study for conducting exposure response analysis.

Overall, OEHHA found that of all the models evaluated, the two-piece linear spline model selected by U.S. EPA fit the underlying NIOSH data best. An updated literature search was conducted by OEHHA for studies published after U.S. EPA's 2016 assessment, and no additional information was identified to necessitate changing U.S. EPA's IUR.

[SLIDE CHANGE]

DR. WOODS: The Steenland et al. publications are based on the NIOSH retrospective cohort study, which included 17,530 workers from 13 facilities across 11 states. The NIOSH study had the largest existing cohort of ethylene oxide-exposed workers, including both men and women and representing 461,000 person years of observations. The absence of potential confounding exposures added to the strength of this study.

OEHHA deemed this study high quality for several reasons, including the availability of quantitative exposure estimates for individual workers, the large cohort size, the multiple study locations, and the results

of our assessment of the study using the Bradford Hill guidelines for causal inference and the National Toxicology Program's Risk of Bias Tool.

[SLIDE CHANGE]

DR. WOODS: The workers included in this study were involved in sterilizing medical supplies, treating spices, and manufacturing and testing medical sterilizers. Mortality, including lymphohematopoietic cancer mortality, and in particular, mortality of lymphoid cancers including non-Hodgkin lymphoma, myeloma, and lymphocytic leukemia were assessed in males and females, as well as breast cancer incidence in females.

The cohort included all employees who worked at one of the facilities for at least three months for mortality analyses and at least 12 months for breast cancer incidence analyses. Mortality and cancer and mortality follow-up was through December 31, 1998 or the date of death, the date of diagnoses for breast cancer, or the date of loss to follow up, whichever occurred earlier.

[SLIDE CHANGE]

DR. WOODS: Workplace air measurements were taken between 1976 and 1985 from 18 different sterilizer facilities and included 2,700 time-weighted personal breathing zone exposure values from workers. Individual exposure estimates for exposures occurring before 1976

were determined using a regression model, which was validated against independent data. The model incorporated information about the facility, the exposure category, and the time period. Factors included in the model were proximity to exposure source, product type, size of sterilization unit, engineering controls, days after sterilization, and calendar year. The model explained 85 percent of the variation in an independent set of 205 ethylene oxide measurements, and the model outperformed predictions from an expert panel of 11 industrial hygienists.

[SLIDE CHANGE]

DR. WOODS: So the unit risk estimates developed by U.S. EPA are for extra risk, so meaning the risk above background. For the calculation of extra risk, we would compare the lifetime risk of developing lymphoid or breast cancer in the exposed population to the lifetime risk of developing the same cancer in the unexposed population. It's the risk in the unexposed population that is considered background risk. These risk estimates are calculated using a life table analysis, which accounts for competing causes of death, and the fact that baseline rates of lymphoid cancer can vary by age. The risks were calculated for continuous exposures from birth to age 85.

Conversions were made to account for the

differences likely to be seen between the occupational exposure estimates used in the NIOSH study and the environmental exposures that are expected to be seen in the general population. These included differences in the number of days, including 240 days per year for occupational exposure rather than 365 days per year, and differences in the average breathing rate by using 10 cubic meters per day for occupational exposure, as compared to 20 cubic meters per day for the general population.

[SLIDE CHANGE]

DR. WOODS: For their assessment, U.S. EPA worked with the NIOSH study authors to perform further analyses including additional exposure response modeling of the NIOSH data. That work included performing linear and long-linear -- log-linear exposure response modeling, weighted linear regressions of categorical data, and linear regression spline models. Spline models allow the slope to change at one or more points called knots along the exposure range.

In addition, the analysis examined different lag periods and mathematical transformations of the exposure variables. Of all the models examined, U.S. EPA determined that the two-piece linear regression spline model with a knot at 1,600 ppm-days provided the best

biologically plausible fit to the NIOSH study data, especially in the lower exposure region using cumulative exposure and a 15 year exposure lag.

OEHHA used the publicly available categorical data to independently evaluate several exposure response models, included weighted linear regressions, weighted least squares regressions, and generalized least squares regressions. Overall, OEHHA found that none of the models provided a better fit to the study data than the two-piece linear spline model used by U.S. EPA.

[SLIDE CHANGE]

DR. WOODS: This is Figure 6 from our draft updated IUR document, adapted from U.S. EPA 2016 Figure 4-9, and it shows the relative risk estimates for lymphoid cancer from occupational cumulative ethylene oxide exposures with a 15 year lag. Of note, this figure does not show the categorical data point for the control group, which would be at a relative risk equal to one.

The two-piece linear spline model with the knot at 1,600 ppm-days is represented by the solid black line. Spline models are useful for exposure response data like that seen for occupational exposure to ethylene oxide, where the relative risk initially increases with increasing exposure but then plateaus at higher concentrations.

[SLIDE CHANGE]

DR. WOODS: This figure is adapted from U.S. EPA Figure 4-3 and shows the same categorical data points and includes both the control group and an additional high exposure group at 40,000 ppm-days. This figure shows the fit of some of the other models to the data. In this figure, the two-piece linear spline model with a knot at 1,600 ppm-days is shown by the red dashed line or the sixth model up from the bottom. The other models give slopes that appear to dramatically over- or under-predict the actual study results, especially in the low-dose range.

In 2020, the Texas Commission on Environmental Quality, or TCEQ, published a risk assessment document for ethylene oxide in which they calculated a unit risk factor that's about 2,000 times lower than U.S. EPA's value. TCEQ did not use a two-piece linear spline model and instead used a Cox Proportional Hazard model, shown here as the solid light blue line at the bottom of the figure. U.S. EPA also evaluated the Cox Proportional Hazard Model and found that it had a poor fit, especially in the lower exposure region, which is more relevant for the general population.

In addition, when estimating the number of cases expected in the NIOSH cohort, TCEQ used external analyses

using the general U.S. population, rather than internal analyses of comparable unexposed workers. This calculation would not account for differences that might exist between the general population and the NIOSH worker cohort. I should note that the TCEQ value is based on the NIOSH data set for lymphoid cancer data only and does not include the second endpoint of breast cancer incidence included in U.S. EPA's analysis, which I'll show in the next few slides.

[SLIDE CHANGE]

DR. WOODS: The IUR was calculated as the lower 95 percent confidence limit of the exposure concentration corresponding to an extra risk of one percent, or the EC01. This was done using a life table analysis, which accounts for the baseline rate of lymphoid cancers, and the slope of the lower spline segment below the knot at 1,600 ppm-days. The analysis resulted in an LEC01 of 1.9 times 10 to the minus three per ppm, and a cancer IUR for lymphoid cancer of 5.26 per ppm. OEHHA replicated the life table and IUR calculations and obtained the same results.

[SLIDE CHANGE]

DR. WOODS: For the breast cancer incidence data, U.S. EPA also evaluated the exposure response relationship using a combination of linear and log-linear models,

models using continuous or categorical exposure data, regression splines, models with and without exposure variable transformation, and models using different exposure metrics, such as cumulative exposure, exposure duration, average, and peak. U.S. EPA selected the two-piece linear spline regression model with individual exposure data, cumulative exposure, a 15-year exposure lag, and a knot at 5,750 ppm-days. OEHHA evaluated several other exposure response models and none of the models resulted in a better visual fit or had lower p-values than the two-piece linear spline regression model selected by U.S. EPA.

[SLIDE CHANGE]

DR. WOODS: This is Figure 7 from our draft document, adapted from U.S EPA figure 4-10, and shows the relative risk estimates for breast cancer incidence from occupational ethylene oxide exposures with a 15 year lag. The categorical data are shown by the purple circles. The two-piece linear spline model with a knot at 5,750 ppm-days is shown by the black solid line. This model had a low p-value and a good visual fit, especially in the lower exposure ranges.

[SLIDE CHANGE]

DR. WOODS: U.S. EPA also applied the life table approach to breast cancer incidence to determine risk

estimates. Again, the lower slope of the two-piece spline model was used to determine risk at lower exposures, as estimated by linear extrapolation of the lower 95 percent confidence limit of the exposure concentration corresponding to an extra risk of one percent. The slope of 8.98 times 10 to the minus five excess relative risk per ppm-days was about eight times lower than the corresponding slope for lymphoid cancer mortality. The LEC01 was 6.75 times 10 to the minus three ppm and the IUR was calculated as 1.48 per ppm.

[SLIDE CHANGE]

DR. WOODS: Total cancer risk estimates were determined by combining the cancer risk estimates for lymphoid in both sexes and breast cancer in females. U.S. EPA stated that cancer risk estimates are intended to reflect total cancer risk and not site-specific cancer risk. Therefore, an additional calculation was made to estimate the combined risk for incident lymphoid and breast cancers because females would be at risk for both types of cancers. Using this approach yielded a final combined cancer IUR estimate of 6.1 per ppm, or 3.3 times 10 to the minus three per microgram per cubic meter. Lymphoid cancer contributed about 75 to 80 percent of the total. And this IUR value describes the excess cancer risk associated with inhalation of one microgram of

ethylene oxide per cubic meter of air.

[SLIDE CHANGE]

DR. WOODS: The corresponding cancer slope factor, also known as the cancer potency factor, is calculated as shown by multiplying the IUR by the reference human body weight of 70 kilograms and a unit conversion factor, and then dividing by the reference human breathing rate of 20 cubic meters per day. This yields a cancer slope factor of 12 per milligrams per kilogram day.

[SLIDE CHANGE]

DR. WOODS: The IUR describes the excess cancer risk associated with exposure to one microgram of ethylene oxide per cubic meter of air, while the cancer slope factor describes the risk associated with exposure to one milligram of ethylene oxide per kilogram of bodyweight. Excess risk describes the risk above background risk. For the purposes of the Hot Spots Program, the IUR is meant to estimate risk associated with exposure to ethylene oxide resulting from facility emissions and does not describe the risk associated with endogenous or background exposures.

[SLIDE CHANGE]

DR. WOODS: So that concludes my part of today's presentation. So I'll turn it back to Dr. Krishnan to

guide us through any clarifying questions or initial input from the Panel on our draft document and to take us through the second part of our presentation.

PANEL MEMBER RITZ: So this is Beate Ritz. I am the main reviewer. I'm a little confused. Cort, can you clarify should I give my review now or wait until the end?

CHAIRPERSON ANASTASIO: Excellent question. Dr. Krishnan, you wanted to give some -- you're going to have additional slides, right?

DR. KRISHNAN: Yeah, I do.

CHAIRPERSON ANASTASIO: Would you prefer we wait until the end of the entire presentation?

DR. KRISHNAN: Yes. If the Panel agrees, we could complete the rest of the presentation, unless you want to...

CHAIRPERSON ANASTASIO: Yeah. I think We're going to get into -- well, let me ask this of the Panel. Does anyone have any kind of big picture comments based on Dr. Woods's presentation. I think we'll save the detailed discussion of Panel comments till the end of the entire OEHHA discussion or presentation.

PANEL MEMBER BESARATINIA: I think it's a -- this is Ahmad. I think it's a good idea to have the presentation continue, because many of the questions that at least on my end I have, looking at this slide set that

was sent to us yesterday, I think they will be covered in the next presentation.

CHAIRPERSON ANASTASIO: Yes, I agree. Obviously, there's a lot of communication between the two parts of the presentation.

So based on that, why don't we wait. Thank you, Beate, for raising the question. We'll wait. We'll have Dr. Krishnan finish the presentation and then we'll go to lead reviewers and then the rest of the Panel.

DR. KRISHNAN: Thank you.

CHAIRPERSON ANASTASIO: So, Dr. Krishnan, please continue. Thank you.

DR. KRISHNAN: Thank you. Now on -- thank you, Dr. Woods. Now, onto the next part of the presentation on the public comments received on our initial considerations on these topics.

[SLIDE CHANGE]

DR. KRISHNAN: At the end of the public comment period as of June 14th, OEHHA received comments from eight stakeholders as shown in this slide. The full text of the comments can be viewed at our website as shown at the bottom of the slide.

[SLIDE CHANGE]

DR. KRISHNAN: OEHHA would like to Panel's input and discussion on public comments covering four topic

areas: One, background exposures; two, study selection for dose response assessment; three, dose response modeling; and four, IUR development and application.

Under these four topics, we will bring forth some of the issues raised in the public comments for which we would like SRP's input and discussion.

We also received comments on other topics including risk management issues, but our focus today is on the IUR factor development and the underlying science. OEHHA will develop full responses to all comments received, including those received at this meeting and present to SRP at a future meeting.

[SLIDE CHANGE]

DR. KRISHNAN: Now, the first topic area we want to focus on relates to background exposures.

[SLIDE CHANGE]

DR. KRISHNAN: The public comments raise the issue of background ethylene oxide levels, or EtO levels, as to how they are accounted for in IUR development and what the implications are, given that most of the background would appear to come from endogenous sources, as we saw in Dr. Woods' presentation, you know, through ethylene from bacterial metabolism, lipid peroxidation, and oxidation of methylene.

[SLIDE CHANGE]

DR. KRISHNAN: This slide shows conceptually how background can affect the observed dose response. Consider this hypothetical dose response, or exposure response, curve for ethylene oxide. On this figure, the zero represents no exposure to ethylene oxide, no exposure from external sources, and no exposure to ethylene oxide from endogenous sources that we just mentioned. But people, including the workers in the study on which the ethylene oxide IUR is based, are exposed to both ethylene oxide generated by their bodies and ethylene oxide from ambient sources. That has the effect of translating the axis on the dose response curve. So this new purple zero on the curve represents exposure above the background. So the IUR, or the slope factor, is derived based on exposure above the background, as we see here.

[SLIDE CHANGE]

DR. KRISHNAN: The ethylene oxide IUR was derived from the epidemiological study. With that in mind, if we look at this triangle here in this pictorial, the upper right hand -- the upper right corner of the rectangle -- did I say triangle. I was going to say rectangle.

(Laughter).

DR. KRISHNAN: I wanted to get their attention.

So looking here, the rectangle here, the upper right hand -- the upper right corner of the rectangle -

well, essentially on the X axis, right - represents zero occupation exposure and corresponding to zero extra risk. That is a relative risk of one. So an exposure value of zero represented no workplace exposure about the background and the relative risk of one represented no increase in risk above the background level in the referent exposure group, but the shape of dose response relationship in the region of background exposure to ethylene oxide that is endogenous or ambient exposures in the occupational study is unknown. That's what we see within the rectangle. So the shape there is essentially unknown and there's a large uncertainty in this region.

And OEHHA doesn't recommend using the IUR to predict the cancer risk from background concentrations in this region. For calculating the additional risk related to facility emissions, it should be done on the basis of concentrations above the background. Now, let's see the broken dashed line above the rectangle there. So the broken dashed line above the background level represents exposure above the background and risk over the background.

[SLIDE CHANGE]

DR. KRISHNAN: You have heard earlier that the cancer potency estimate or IUR for ethylene oxide was derived from the NIOSH study based on occupational

exposure above the endogenous and ambient background levels and it was based on risk level above the background.

So in the calculation, the IUR was based -- was derived by accounting for background risk of lymphoid cancer and breast cancer, which are on the order of three percent and 15 percent respectively, in the US population in terms of background lifetime incidence.

[SLIDE CHANGE]

DR. KRISHNAN: So we OEHHA is thinking for modifying the draft IUR document along the lines of clarifying further that the IUR is based on risk above background and that it is for use in risk calculations for exposure concentrations above background resulting from facilities emissions.

[SLIDE CHANGE]

DR. KRISHNAN: That's about the issue on the background exposures. I can pause here if there's any initial comment or a question before moving on to the next topic area.

[SLIDE CHANGE]

DR. KRISHNAN: So the second topic area relates to the study selection for dose response assessment.

[SLIDE CHANGE]

DR. KRISHNAN: As we saw earlier in the

presentation, OEHHA and EPA used the NIOSH cohort study as the key study for conducting the dose response assessment for ethylene oxide. Issues have been raised regarding the consideration and use of this particular study and not others, as well as the validation of the exposure model of this study.

[SLIDE CHANGE]

DR. KRISHNAN: OEHHA thinks that the NIOSH study is the best available study for conducting exposure response analysis for ethylene oxide. We agree with the EPA's selection of this study for analysis. During our review, we did not identify any new studies that would result in a better estimate of IUR for ethylene oxide. The high quality of this study differentiates it from other studies, for example, the Union Carbide cohort study, which was raised in the comments, and which has several weaknesses compared to the NIOSH study in terms of smaller sample size, unclear accuracy of exposure assessment, potential for unaccounted and important co-exposures, failure to include women, and failure to account for a lag between exposure and disease onset.

The reliability of expose -- of epidemiological studies for dose response assessment depends upon whether or extent to which they take into account and address these important issues.

On regarding the NIOSH exposure regression model, OEHHA's considerations were based on the many exposure measurements made, as well as the evaluation of the model performance that Dr. Woods alluded to earlier.

And for the earlier years in the study when the exposure measurements were not available, there was information on other important exposure factors that were available and used to estimate exposure. So OEHHA considered these strengths of the exposure modeling in its consideration of the NIOSH study as the key study for this assessment.

[SLIDE CHANGE]

DR. KRISHNAN: Now, onto the third topic area. Of the dose response modeling based on this critical study, there were many comments covering three general areas, the model development, model selection, and model evaluation.

[SLIDE CHANGE]

DR. KRISHNAN: As indicated earlier, OEHHA concluded that U.S. EPA's two-piece linear spline model provides the most appropriate and best fitting model for assessing the cancer risks of ethylene oxide.

Issues were raised in public comments that focused on: individual NIOSH study data not being available to conduct an independent evaluation; the use of

categorical data to assess the model fit; and the two-piece spline model in terms of minor differences in calculating variance leading to small changes in p-values.

[SLIDE CHANGE]

DR. KRISHNAN: Although OEHHA did not have the individual study data, key information was available to evaluate the quality of the cohort study and the dose-response relationship. OEHHA was able to evaluate a number of exposure-response models using the publicly available categorical data provided in either Steenland et al. or the U.S. EPA documents.

Further, OEHHA considers that the categorical data or results were calculated using long-standing and widely accepted methods. As such, they've been considered to be valid both by U.S. EPA and OEHHA.

[SLIDE CHANGE]

DR. KRISHNAN: On the topic of model selection, OEHHA considered that the statistical approach used was by the authors was based on widely accepted and appropriate methods. And the model selection was based on several considerations: evaluations of bias and causal inference; parsimony; biological plausibility; differences between higher and lower dose effects; p-value as well as other statistical considerations. Thus, OEHHA and U.S. EPA considered a number of factors in addition to p-value in

model selection.

[SLIDE CHANGE]

DR. KRISHNAN: As referred to in the public review draft and early by Dr. Woods, the Texas Commission on Environmental Quality, TCEQ, also conducted dose response modeling for ethylene oxide. The cancer slope they generated is about 2,000 times lower than that of the U.S. EPA value and our proposed IUR. This point was raised in the public comments.

And as you hear earlier, TCEQ chose a different model, the Cox Proportional Hazards Model. And this model is inconsistent with the underlying epidemiological does response data, as shown in slide 19 of Dr. Woods presentation. Furthermore, the reality checks by TCEQ did not account for healthy worker effect and related effects.

[SLIDE CHANGE]

DR. KRISHNAN: The next set of issues raised on dose response modeling relate to a reality check based on background levels using the IUR and using hemoglobin adducts for conducting and communicating the risk assessment for ethylene oxide.

[SLIDE CHANGE]

DR. KRISHNAN: As noted earlier, the derivation of the IUR for ethylene oxide is based on extra risk, risk level adjusted for background incidence. So it is for

estimating the extra risk resulting from exposure to facility emissions over and above the background.

OEHHA did not use the IUR based extra risk to calculate the background risk to do a reality check, especially for endogenous levels of ethylene oxide because of large uncertainty in such an application.

So I intended this figure to show that, you know, the IUR is based on extra risk. And to do -- doing a reality check, you know, based on the IUR based on the extra risk to interpret endogenous levels of ethylene oxide is something that OEHHA did not do because of large uncertainty in such an application. So I intended to say while I kept changing the slides back and forth. Sorry about it.

I touched the wrong button.

[SLIDE CHANGE]

DR. KRISHNAN: So on this topic, OEHHA considers that it is unreasonable to use endogenous levels for reality check because of the unknown contribution of endogenous levels of EtO and other factors to the baseline risk. And the IUR is for calculating cancer risk above the baseline and for EtO exposures above the background.

And for the issue on hemoglobin adducts. While the hemoglobin adducts, specifically the hydroxyethylvaline adduct, or HEV, are useful as

biomarkers of ethylene oxide exposure and they integrate exposure from all sources of ethylene oxide in all -- including endogenous and exogenous exposures. But due to the paucity of data on the relationship with the relevant internal dose metric for carcinogenicity makes them a limiting factor for use in dose response assessment and risk assessment.

[SLIDE CHANGE]

DR. KRISHNAN: The next set of issues raised in comments on dose response relate to mechanistic considerations. So you see two here.

An issue raised in the public comments is that the steep initial dose -- initial slope of the two-piece linear spline model is not justified by evidence from animal cancer bioassays on genotoxicity data. And despite the clear evidence that ethylene oxide is genotoxic and carcinogenic issue has been raised that it does not necessarily mean that ethylene oxide actually is a genotoxic mode of action for its carcinogenicity. So it's a mode of action question on carcinogenicity in relation to the model used in this assessment.

[SLIDE CHANGE]

DR. KRISHNAN: Regarding the justification of the two-piece linear spline model, as mentioned earlier, OEHHA evaluated several exposure-response models using the

publicly available categorical data provided in Steenland et al. and the U.S. EPA documents. And overall, OEHHA found that none of the models it evaluated fit the underlying NIOSH study data as well as the two-piece linear spline model. This model is also consistent with the low dose linearity assumption that is the default assumption used in dose-response modeling. That assumption contained in the Hot Spots guidelines reviewed and approved by the SRP.

And regarding the mode of action issue, both OEHHA and U.S. EPA agree that there is sufficient weight of evidence to support a mutagenic mode of action. That being said, the draft IUR was derived using human cancer epidemiological data. And knowing the mechanism is not a prerequisite for using the human data to drive an IUR.

[SLIDE CHANGE]

DR. KRISHNAN: I would pause here to take any questions or any initial comments about the selection of the study and model selection before going to the final topic.

[SLIDE CHANGE]

DR. KRISHNAN: The fourth and final topic covered by the public comments as represented here relate to IUR development and application.

[SLIDE CHANGE]

DR. KRISHNAN: OEHHA received comments regarding the selection of the IUR value after the dose-response modeling conducted by EPA. EPA's analysis provided two values, an initial value of 3.3, 10 to the minus three per microgram per meter cubed based on consideration of age-independence of relative risks in the analysis. And that was used in OEHHA's public review draft.

And then there was a recalculated value of three 10 to the minus three in EPA's document, which is 10 percent lower. It's a recalculated value, which is compatible with the application of age-specific factors.

While the first one assumed risk being independent of age, the second one accounted early life susceptibility. And we now believe that the final EPA number of three, 10 to the minus three micrograms per meter cubed is the appropriate value to use. This is because this number can be used directly with the Air Resources Board's HARP, the Hot Spots Analysis Software Program, within which age-specific -- the age sensitivity factors are integrated for conducting facility health risk assessments.

[SLIDE CHANGE]

DR. KRISHNAN: An issue raised during the public comments under this area is there's a difference in the cancer risk estimates using the hot spots methodology

versus EPA's risk estimates for ethylene oxide. But this is not an ethylene oxide-specific issue as we looked into it. And it really related to the calculation methodology, one being based on air concentration and the other being based on inhaled dose. The inhaled dose calculation takes into account not only the exposure concentration, but also the age-specific inhalation rate and body weight has done under the hot spots methodology. And this methodology has previously been reviewed by the SRP.

And as I mentioned, you know, the outcome based on -- calculation based on directly the concentration are the one based on dose accounting for inhalation and body weight is not specific to ethylene oxide.

So with that, we look forward to the Panel discussion and input on the initial -- on the public review draft and these four issues or topic areas that I presented and any additional thoughts including thoughts about further clarification of the use of IUR under the Hot Spots Program in this document on ethylene oxide. And before I turn it over to you Chairman Anastasio, I briefly want to go over the next steps, if you would permit me to do so.

CHAIRPERSON ANASTASIO: Yes, please go ahead.

[SLIDE CHANGE]

DR. KRISHNAN: So after the meeting today, OEHHA

will continue to consider and develop written responses to public comments received so far and at this meeting. We'll revise the draft in consideration of these public comments, and the SRP's input at this meeting, and then OEHHA will bring the revised draft SRP for review at a future meeting.

Thank you.

CHAIRPERSON ANASTASIO: Great. Than you, Dr. Krishnan. Thank you, Dr. Woods.

Let's start with our lead reviewers. Beate, would you like to go first?

PANEL MEMBER RITZ: Yes. So I reviewed this document and I specifically emphasized, of course, the epidemiology, because I'm an epidemiologist, but I reviewed everything. I thought it was really well written in general. However, I have a lot of wording issues with the epidemiology parts, so I will -- I will give you all of these wording issues, and, you know, we can discuss why I think you should possibly consider rewording certain sentences, because they're not up to date anymore with how epidemiologists talk about studies.

I don't think I need to give you my list right now of these kind of wording changes. For example, one was sensitivity. You call studies more sensitive. That's not -- sensitivity in epidemiology has a very special

meeting. You probably want to reword that slightly.

Generally, I think the epidemiology is actually quite strong in the sense that this NIOSH study was extremely valuable and a strong study. So I went back to the original study, read it in detail, and came up with my own evaluation. And I, as an occupational and environmental epidemiologist, I have to say I've rarely ever seen such a great piece of work in a human study, especially when it comes to the exposure assessment with so many measurements, the regression analysis they used in order to determine individual level exposures for all of these workers, but also the analysis that tried a lot of different lagging methods.

And, in general, the way how critical and self-critical the writers of this study actually were in terms of trying to go down every road to find out whether there's bias. So I think the NIOSH study is really the strongest study of the bunch, but it's also, in general, really a strong study. And I completely agree with using that study for the IUR development.

In terms of the -- in terms of the slope that was used, the spline models, spline models are very common in epidemiology. Every time my students come with a dose response, we start with categories. And then I say, well, why don't you try a spline model, because they are, you

know, quite strong in identifying these difference slopes at different levels of exposure. And this is not unusual that you're not just using one parameter when you don't have enough data for completely nonparametric estimation, that you're using a spline model and that you're getting results like this. Actually, I've done radiation studies before and there's a very good example where carcinogenicity of upper radiation has a very steep slope in the beginning and then cell killing starts.

And, you know -- and so the slope basically flattens out. So that's a biologic example of another type of exposure where we see a lot stronger risk for cancer in the lower end of the exposure curve. And then at the higher end, and I mean everybody knows they are using radiation to treat cancers, right, because it's cell killing at the higher end of the radiation exposure you see this flat line or even the risk going down eventually. So that didn't surprise me at all and I think what we've seen about all of these slope factors was quite convincing here.

What else?

There was one other study I think that could be considered a little bit more in support of the low exposure risk for breast cancer at least. That was the Swedish study where the authors looked at only one company

that used a sterilization method with EtO and had a lot less workers and a lot less well done exposure assessment, but otherwise a pretty strong data set, because the Swedes have cancer registries. And that study actually suggested a very strong risk for breast cancer in the lower end of the exposures, but basically didn't have any higher exposures to play with, so they can't really tell you what's happening at higher exposure levels. But maybe that could be emphasized a little bit more that there is another study actually in support of that higher risk at lower ends.

I also agree that studies that have been published recently that use the Toxics Release Inventory or some EPA NATA models for population risk are really not useful. They are conforming, but possibly confirming the hazard, but they're not really useful for this IUR development. So they're possibly just in support of what we've seen here, usable in that way.

The issue of above -- excess risk above background, I mean, that's what epidemiology does. That's our bread and butter. There's no question that that's the right way to do it. We are always comparing additional exposure above the background risk, so that's nothing new.

Was there another question that we were asked to answer that I forgot?

CHAIRPERSON ANASTASIO: Dr. Krishnan, maybe you could share your last slide again that had the issues you wanted to discuss.

DR. KRISHNAN: Yes. Hold on.

CHAIRPERSON ANASTASIO: Great. Thank you.

PANEL MEMBER RITZ: Oh, yeah. So -- oops. Now, I can't see it anymore.

Ah, it's coming.

Yeah, so adopting EPA's final value I think it's a good idea, because leukemia, not breast cancer, but leukemia definitely and lymphoma are childhood cancers or seen in childhood as well, and they might be susceptible age groups, so I agree with that.

And the last point, I don't have anything new.

CHAIRPERSON ANASTASIO: Beate --

PANEL MEMBER RITZ: And as I said, I have -- I have editorials on the way that the epidemiology is described, but I'll hand that in.

CHAIRPERSON ANASTASIO: Yeah. That's great. Thank you for your comments. I had a follow-up question for you, Beate. You talked about having read the NIOSH study. Can you talk about this issue of the modeled exposures pre-1978? Did you form an opinion about that?

PANEL MEMBER RITZ: Yeah, I actually really liked that, because I developed similar kind of models with my

colleagues at UCLA that we use -- that we are using in air pollution epidemiology. They're called land use regression models. And they're basically the same of what these offers here have done. What you do is you use everything you know about features in the workplace or in the environment that contribute to exposures. So in the case of, for example, air pollution, that would be how many cars go down a road, what the land use is of that part of the area that you're trying to evaluate air pollution in what -- you know, how -- what the fleet composition is, whether they are trees, et cetera, et cetera.

And then you are measuring air pollution at one point or multiple points across an area and you're trying to use everything -- every source of exposure that you know is a source of exposure to predict the actual measured value. And that's what we call a land use regression and generally an R square of -- above 0.8 is considered exceptionally good. And what these authors did here is basically the same thing. They knew about the job titles. They knew about equipment. They knew about how this equipment was used and other engineering controls.

And then they had 2,700 measurements, which is a lot. And they tried to use all of what they knew about the workplace to predict the actual measured level in the

workplace. And they got an R square of more than 0.8. And that's -- and with that, you now can use this regression model to actually predict every worker's individual exposure if you know where you worked, because you have all of these variables that predict -- that predict the level of exposure and you can regress that value on every worker.

And I think that's a very strong way to do it. And they try to do the same thing by asking industrial hygienists to actually predict these kind of exposures and their regression model outperformed the predictions of these very knowledgeable exposure assessors in the workplace. And I'm actually not surprised that they did.

CHAIRPERSON ANASTASIO: That's great. Thank you. Yeah, thanks very much for your comments.

I'd like to turn it over now to Dr. Messer our expert statistician.

PANEL MEMBER MESSER: Thank you, Cort.

Yeah, so I think what will be most useful is if I can provide some written discussion of some of these technical issues. I think that might be most helpful to clarifying some of these points.

In general, I agree with the comments of Beate that I think she gave a very nice summary of the methodological strengths of the underlying paper and of

the appropriateness of the general approach of a linear spline model, especially when trying to assess exposure risk -- the exposure risk relation in a particular region, in a low-dose region, so above the background. So you're looking at additional exposures, but within a plausible range of exposures, not at very, very high exposures, such as might not be experienced in the -- in this setting. It's appropriate to use a model that uses the data in that region that you're interested in to infer the slope. And that's what align a linear spline model does.

So it's like -- it mimics a regression just over the region of interest and it allows the higher values to have some influence on this area that you're interested in, but it limits the inference specifically to the area that you're interested in in your model. So it's a very appropriate methodology and I find the graphs generally quite convincing, especially for ruling out the Cox proportional hazards model. I'd like to read that model a little more carefully to make sure I understand what it's doing and then I'll give some technical comments on why I think the fit is so poor of the Cox proportional hazard model.

I'll provide some comments on the way the model comparison was done. And again, I may have some technical comments there, but I think generally, it's quite

appropriate. And generally there's a clear lack of fit of many of those models, but I may have some suggestions for how to conduct that kind of model comparison assessment. I agree with the main approaches assessing bias considerations of causal inference, biological plausibility, parsimony. Those are all valid and then the basic assessment of fit to the data.

I'd like to read the public -- the technical public comments. I understand there were comments on how the variance was calculated and other technical comments. So I'll read those comments and provide a technical response to them. But generally, this looks like a high quality -- a high quality approach based on -- as Beate pointed out, based on high quality data.

CHAIRPERSON ANASTASIO: Thank you, Karen. I know you want to get into more detail in your written comments, but can you give us a summary of why the Cox proportional hazard model isn't a good fit.

PANEL MEMBER MESSER: My guess is because they didn't -- because the underlying hazard is modeled as a completely linear hazard. My guess is that's what they did. You can use a two-piece linear spline model to model the hazard in a Cox regression, and likely that would have been more appropriate and likely that's not what was done. So that's what I'd like to just double check.

You know, I think a Cox proportional hazards model, I have to see the specifics of how they applied it, but that model itself might be quite appropriate. It's just they didn't model the risk appropriately. They probably used just a linear regression, which as we've seen from the other -- the other models presented doesn't fit the data very well. So I think that's what's going on.

CHAIRPERSON ANASTASIO: Okay.

Thank you. Any other comments?

PANEL MEMBER MESSER: No. I think -- I think that's it. I agree with the main points of the presentation, that -- especially the idea that the spline model is an empiric -- an empiric fit to the risk data. That's what's required of a model like this. So the comments that there's not a mechanistic support for that particular kink, I don't think that's necessary. It's an empirical fit to the risk that's important here.

And just another comment about this idea of back extrapolating from the spline model into the area of endogenous exposure. I agree with the comments by OEHHA that that would not be an appropriate use of this model that was developed exclusively on the excess risk data.

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

I'm going to now -- we'll go through other panelists and I'll ask each person individually to tell us if they have additional comments. I'm just going to go in order on my Zoom screen. So Pam, you're first.

PANEL MEMBER LEIN: Thank you, Cort. I really don't have anything to add to what both Karen and Beate have already indicated.

I agree, I think that the approach used by OEHHA is appropriate. I think the conclusions they reached are well substantiated by the information provided in the report. Yeah. I don't have much to add on the clarification of the use of the IUR under Hot Spots Program. I'm -- I have to become more familiar with the Hot Spots Program, but conceptually it makes sense to me.

So overall, I support the basic premise underlying the approach used by OEHHA and support the conclusions that they've reached.

CHAIRPERSON ANASTASIO: Okay. Thank you.

Ahmad, comments.

PANEL MEMBER BESARATINIA: Yes. I think going through the draft, I found it quite interesting. And I must say that equally interesting was the public comment section, which was quite extensive. This was one of the, I must say, the longest public comments draft that we -- I have seen. There are many valid points in these public

health comments. And I think Dr. Krishnan kind of highlighted them in his presentation. There were at least three or four points that need to be addressed in the revised version. Obviously, just a point-by-point reply, where these comments can be addressed.

I think the three or four main points were the selection of this NIOSH study. Reading through the draft, it appears as if this is a gold standard study and the other two studies have been kind of set aside. I think there needs to be a little bit more information as to why this study was selected. There is very brief -- very brief description in the tables, if I can get that Table 7, I guess -- somewhere in the comment section of Table 7, they are indicating why the other two study, including Union Carbide Corps and the Swedish study was not selected. But perhaps that type of clarification should come in the text.

There was another issue with the selection of models. That is obviously something that needs to be elaborated in the main document.

The other point was the endogenous exposure, the endogenous sources as well as ambient exposure from other sources. So that needs to be, I think, expanded a bit, particularly as we know the tobacco smoke is the single most source of ethylene oxide. So it needs -- I would

like -- I would have liked to see more information on that regard.

There was the issue of healthy worker bias that was raised by multiple commenters on the public comment section. So the use of internal comparison group versus the general population to drive the SMR and SIR. So those are things that would be helpful if the authors put it up front, so it makes it -- it makes it more comprehensive, the draft itself, as well as somehow even-handed. The way that it is -- it reads right now, it leaves the impression that it's a done deal. NIOSH study is the gold standard model is the one that needs to be used, because if EPA used it.

So I would -- I would have liked to have a bit more discussion on that in the draft itself. But other than that, I agree with both Beate and Karen, the main points are highlighted in the draft. I agree with them. It's just some clarification and expansion of the draft itself.

Thank you.

CHAIRPERSON ANASTASIO: Thank you, Ahmad.

Kathy, comments.

PANEL MEMBER HAMMOND: Yes, thank you. I have no further comments. I think it was very good job and I Thank the presenters, and also the -- my fellow SRP

members for their excellent comments.

CHAIRPERSON ANASTASIO: Thank you, Kathy.

Joe, do you?

PANEL MEMBER LANDOLPH: Yeah.

I've gone over it a number of times. I want to put some more time into finalizing my opinions. There was a comment I think it was by the public that even though ethylene oxide is a mutagen, that doesn't mean how it causes carcinogenesis via mutagenesis.

I would kind of take the opposite opinion on it. It's a hell of a mutagen. It's been demonstrated in many systems. That doesn't mean that conclusively settles this by any means, but I'd like to see more data, you know, see actually some data that it could act by a non-mutagenic mechanism before I could accept the way that was written. So I think that should be changed a little bit. I would say maybe the presumption right now, the hypothesis that ethylene oxide is a known, strong mutagen, and that this might be the way or one of the ways that it causes carcinogenesis. I kind of take a tack like that.

I agree with all the comments that everybody made so far, particularly tobacco smoke is a strong source of ethylene oxide. That should be stressed. That ethylene oxide is very mutagenic.

And let's see, what else? I like the dose

response modeling. That was very illustrative with the spline curves and all, and I agree with all that.

And the data on breast cancer is very important. I'd like to see a table maybe at the end when you finish this what's going to be a pretty huge document of the IURs for -- you know, for breast cancer, the leukemias, anything else that is thought to be carcinogenic for and a summary at the end of the document. And I was very impressed by these line spline models too and their ability to predict -- explain the data.

I want to go over the draft document with a fine-tooth chrome and finish my comments and give them to you. And I agree with Ahmad, I think this first draft is very, very interesting. So I like the writing in general. I'm sure it can be spiffed up a little bit, but it's pretty clear. I have no trouble reading this document and understanding it. It's a very well written document, very thighs document, very clear.

CHAIRPERSON ANASTASIO: Thank you, Joe.

So I have some comments, but we're scheduled for a break at 11. And I think it's going to take more than 10 minutes for my comments, so I'd like to take our break now. We'll take a 10-minute break from 10:52 to 11:02. And then we will reassemble, and I'll have my comments, and then we'll get response from OEHHA.

All right. So we'll see you in 10 minutes.

(Off record: 10:52 a.m.)

(Thereupon a recess was taken.)

(On record: 11:02 a.m.)

CHAIRPERSON ANASTASIO: Okay. We're going to restart everybody.

Excuse me. I'm going to wait for Joe and Karen to return.

Excellent. Okay. So I wanted to express my comments. The first one was that, you know, we talked about this model of leveraging information from other agencies like EPA and the development of health guidance values with the hope that it would save time. And I'm just wondering for Dr. Woods and Dr. Krishnan, did it save significant amounts of time?

DR. KRISHNAN: I think the intent was not to directly adopt without any evaluation or going through.

CHAIRPERSON ANASTASIO: Oh, sure, right. No. No. I wasn't suggesting that, but you know it wasn't as time-consuming I imagine as a typical IUR would be. And is that true? Did this -- did this new process save time?

DR. KRISHNAN: In this particular case and for this chemical from my limited experience, yes, OEHHA, I would say, you know, no, it didn't -- it did?

DR. WOODS: Yeah.

DR. KRISHNAN: Because I think normally, it had taken even longer or could I ask --

DR. STEINMAUS: I mean, for me, who was involved in selecting this study, it was just such a high quality study that I didn't -- and the evaluations were so -- and not just in the papers themselves, but in the 2016 update by Kyle Steenland. It was just such a high quality, intense, comprehensive evaluation, that it was easy to go with that study and that data.

CHAIRPERSON ANASTASIO: I see. So a confounding factor in understanding the impact of the process versus this very good study. Okay. Thank you.

My second comment is about this question of whether EtO concentrations are elevated near sterilization and other point sources. And some of the public comments were suggesting that they were not, which would seem odd, but it really depends on the lifetime of EtO in the atmosphere. So I thought it would be helpful if you could add just a sentence or two about the lifetime of EtO, which from my reading is on the order of days, which would suggest that you should see a pretty strong gradient of significantly higher concentrations in your sources.

My second comment was about Figure 6. Can -- Dr. Woods or Dr. Krishnan, can you show -- can you share your screen with the Figure 6 with all the different fits on

it? I think you had two versions.

DR. WOODS: Sure. Let me get that pulled up for you. Give me just a second.

CHAIRPERSON ANASTASIO: Yeah. And actually the next one. Let's look at the super busy one. Yeah.

So first comment is, this is categorical data. The individual data you mentioned is not available. I understand it's thousands of data points, but that's not available?

DR. STEINMAUS: Well, we probably could have asked for it. Steenland makes a comment in his 2016 evaluation that he no longer had access to it, because he wasn't at NIOSH any more. So I suspect it would have been very difficult, if not impossible, to get, but the bottom line is we didn't feel like we needed the individual data, since the evaluations that Steenland had done for U.S. were so comprehensive.

CHAIRPERSON ANASTASIO: I see. I'm not familiar with using categorical data. I'm not a statistician, but is there generally no expression of variability on categorical data? Like I would -- if my group was showing me data, I would expect error bars.

DR. STEINMAUS: Well, most -- the lines are actually continuous data, not categorical. And then the dots are the categorical data. So you're absolutely

right, this is from U.S. EPA and they certainly could have put in the 95 percent confidence intervals. And maybe they should have on the -- on the categorical data, the dots, but I think that would have just made this slide way too busy. They did present those 95 percent confidence intervals in their -- in their report.

CHAIRPERSON ANASTASIO: I remember seeing that.

DR. STEINMAUS: So I got a note that I should introduce myself. So I'm Craig Steinmaus. I'm an epidemiologist and physician at OEHHA.

CHAIRPERSON ANASTASIO: Great. Thank you for introducing yourself and thank you for your responses.

Okay. Right. I'm remembering now. The categorical confidence intervals are in the table. Okay.

I'd like to try to understand better this 2,000-fold difference in the OEHHA IUR, in the Texas CEQ IUR. Was this the slide that has the TCEQ fit is one of those blue lines at the bottom?

DR. STEINMAUS: Yeah, that's correct. It's the lowest line was the same model that TCEQ used.

CHAIRPERSON ANASTASIO: Okay. Well, I would not call that a good fit to the data. So can you describe to me kind of qualitatively why it is then at very low cumulative exposures there's such a big difference between the spline fit and this Cox proportional hazard fit?

DR. STEINMAUS: Yeah. U.S. -- it's complicated and it would take a long time to explain all of it, but let me -- U.S. EPA had a very good explanation for that in their response to public comments. And we referenced that explanation and gave a brief overview.

The bottom line is that that lower line, the log relative risk Cox proportional hazard model, actually over the entire course of the exposure range is sublinear, which means that it's flat at the bottom at the lower exposures. And then in order to meet -- to come close to the exposures in the higher exposure range, it has to -- it has to curve way up.

So that curve, that sublinear curve, makes it low in the lower exposure ranges, which are what we're seeing here in this figure. So that's why that blue line is so low and it's much different than the categorical data points and much different than the spline model. It's because of that eventual superlinear aspect. Again, you can't see it here, but at the higher exposure doses, it starts curving. It has to curve way up to meet these higher exposure doses.

CHAIRPERSON ANASTASIO: I see. Is it -- so this is EPA data. You don't have abscess to this data?

DR. STEINMAUS: We don't have access to the individual data, you know, the data points on every single

individual in this study. And, you know, it's not just that, you know, NIOSH might not want to give it to us. It's also, you know, privacy concerns. You know, I've done a number of studies and U.S. EPA has asked for my data. And it has taken me a year or two to get our ethics board at UC Berkeley to approve it, so -- because of, you know, personal confidentiality issues.

So, you know, there's difficulties in getting individual data. But again, like I said before, we didn't feel like we needed it.

CHAIRPERSON ANASTASIO: No. Sorry. I wasn't talking about the individual data here. I was talking about the parameters for these regression fits.

DR. STEINMAUS: Yeah. Yeah. We have the regression coefficients and the 95 -- or 90 -- 90 to 95 percent confidence intervals on all of these. Yeah, it's all in the U.S. EPA document.

CHAIRPERSON ANASTASIO: Let me suggest that it might be helpful to show the data either with a blowup of the very low cumulative exposure range, so you can see the difference between the Cox proportional hazard fit, which sounds quite poor in that relevant range, or to show the data -- not -- the data and the fix primarily on a log scale. Just something to show the difference in the cumulative exposure range that actually matters for

environmental exposures, right, because those are way close to he origin, right?

DR. STEINMAUS: Yeah. That would be correct, yep.

CHAIRPERSON ANASTASIO: So being able to -- at least for me, being able to understand why this 2,000-fold difference in the IURs really hinges on what's happening close to the origin, or at least very low cumulative exposure levels.

DR. STEINMAUS: Yeah. And, you know, you can't see it on this graph, because, you know, the blue line obviously at the lower exposure range is below 5,000 obviously is much less steep --

CHAIRPERSON ANASTASIO: Right.

DR. STEINMAUS: -- than that dotted red line. So -- but you make a pretty good point. Maybe we could focus more on that lower exposure region to really show the difference.

CHAIRPERSON ANASTASIO: Right. And, you know, you've got a factor of 2,000 difference, so you almost have to use a log scale to really have that come out.

Other comment related to this figure, you know, in the document, there's some -- oh, wait. Kathy, do you have a follow-up comment on this issue?

PANEL MEMBER HAMMOND: Yeah. I was just going

to -- I like the idea and I was going to suggest you could have another graph that's just showing that lower concentration, and then it could be. And that -- and I think that would be particularly useful. I think that was a good idea, Cort, to have it in the range where we're talking about environmental levels are, you know, and what we're -- you know, so the box could -- it would be informative in the area that's most important and relevant.

DR. STEINMAUS: Yeah. So just expand that lower left section of this graph. Just expand that.

PANEL MEMBER HAMMOND: Well, I guess -- yeah. What I'm suggesting is a second graph that just uses that small area.

DR. STEINMAUS: Right. Yeah. Okay. Yeah, that's a good idea.

CHAIRPERSON ANASTASIO: So on a related note in the document, you discuss that -- why the difference between a TCEQ and the OEHHA IUR. And the first point is, well, TCEQ didn't consider breast cancer, which I agree is an important point, but it's a pretty small factor compared to this factor of 2,000, right. Since breast cancer was responsible for less than half of the incidents of cancer, that's, you know, going to be no more than a factor of two on the IUR I think.

So you had another reason why -- I think it was fit was another reason. My suggestion is put the reasons for the difference between TCEQ and OEHHA in rough order of their importance in terms of explaining this factor of 2,000. And it seems like the fit is the biggest issue. And so I think that needs to go first and I think it needs more discussion. And so this new figure of blowing up the low cumulative exposure data range would help in that description.

DR. STEINMAUS: Yeah, you're a hundred percent right. And I think we put a lot of that in the -- our responses to public comments, but I don't know that we have that much of that in the draft, so...

CHAIRPERSON ANASTASIO: Right. Yeah, there's not much in the document itself. There is some, but --

DR. STEINMAUS: Yeah. Yeah, maybe we could transfer some stuff over, yeah.

CHAIRPERSON ANASTASIO: Karen, do you have a follow-up point on that?

PANEL MEMBER MESSER: Yeah. Just that I agree, it's surprising that, you know, if this is an accurate representation of how TECQ, T-E-C-Q, value was developed, it's very surprising that a model that fit this poorly was used, so -- in the Texas document. So I may go back and look at that Texas document a little -- a little bit to

try to understand how they could have developed a model that fit this poorly.

CHAIRPERSON ANASTASIO: Yeah. It would be --

DR. STEINMAUS: Yeah, I'm really interested in your input. Yeah, I think it's just another of the many, many, many examples of, you know, when you base things solely on a p-value or an AIC score how you can -- it can lead you to some major mistakes, but I'm very interested in your opinion on that.

PANEL MEMBER MESSER: Yeah. And then just a word of caution, you know, if we blowup that lower left-hand corner. I like the idea of putting the Y axis perhaps on a log scale here in this graph. If you concentrate on the low exposure region of X axis, I wouldn't go so far as to exclude those first three data points, because they're driving the models.

CHAIRPERSON ANASTASIO: The first three non-zero exposure.

PANEL MEMBER MESSER: Yeah, those first three purple categorical data points.

CHAIRPERSON ANASTASIO: Yeah.

PANEL MEMBER MESSER: Got to --

PANEL MEMBER HAMMOND: The observed data.

PANEL MEMBER MESSER: Yes. The observed data, not the modeled fits. But if you blow this up, it's still

helpful to include the observed data.

CHAIRPERSON ANASTASIO: Yeah.

DR. STEINMAUS: I probably shouldn't say this, but I just got to -- thank you so much for saying that "observed data," because that was another point that was in the public comments. And I agree with you a hundred percent, those are the observed data points.

CHAIRPERSON ANASTASIO: One final comment related to this. So in one of the written public comments, there were -- they used the regression fits to estimate, I believe it was, the incidence of the lymphoid cancer. And their point was that the TCEQ estimates, based on the TCEQ fit, were closer to the observations in the study than were the OEHHA -- if you took the OEHHA regression and calculated the incidence. Can you address that point?

DR. STEINMAUS: Yeah. What TCEQ did in those calculations was as their reference group, they used the U.S. population as a whole. Steenland, and even TCEQ in their final numbers, they used an internal comparison group, which is much better. So the TCEQ that -- you're referring to their reality check or their ground-truthing exercise. It's most likely biased, because they use that U.S. reference -- the U.S. population as their reference group and not an internal comparison group, so it's probably biased by the healthy worker effect, or the

healthy worker survivor effect, or related issues to that. So that was our point is that that analysis was biased.

CHAIRPERSON ANASTASIO: Okay. And if -- okay. All right. Thank you on that. And then my final comment was -- oh, wait. I see hands. Very exciting here.

Beate, you want to go first.

PANEL MEMBER RITZ: Yeah. I just would like a clarification. I heard something, and I may have been wrong, that the leukemia -- in the presentation, that the leukemias make up the bulk of the cancers. I'm a little bit surprised by that, because it's a rarer disease. And if you increase breast cancer risk by 50 percent or 90 percent, it's usually more cancers than if you would do that same relative risk increase for leukemias, a lot more in attributable numbers. So I just want to make sure that I did not mishear and that that's also reported correctly.

DR. STEINMAUS: Yeah. I mean, obviously, you're absolutely right. Breast cancer did have an important contribution to our -- the overall number. So, you know, certainly lymphoid cancers did too. You know, the relative risks were pretty high. But yeah, they both contributed, both cancers.

CHAIRPERSON ANASTASIO: Karen.

PANEL MEMBER MESSER: Yeah. I'll do this more carefully when I can see the response to the review to the

public comments, but I just wanted a clarification, when TECQ did their ground truthing, were they projecting to U.S. population -- were they fitting to the U.S. population lymphoma rates or to the rates in the exposure study?

DR. STEINMAUS: They were trying to project to -- not the rates, but they were trying to project to the numbers of cases that were seen in the Steenland study. So that -- that was their ultimate goal to try to estimate those numbers of cases and see if it matched what was actually reported.

The problem was was that when they did that, they did like SMR calculations, like we would normally do SMR calculations, where we used the general U.S. population as the reference group. So that was the issue, they used the general U.S. population as opposed to using a group of workers, a group of lesser exposed workers from the Steenland cohort.

PANEL MEMBER MESSER: Okay. Thank you.

CHAIRPERSON ANASTASIO: Beate.

PANEL MEMBER RITZ: Yeah. So basically, they are using the U.S. rates to derive the expected number of cancers in the -- in the cohort.

DR. STEINMAUS: Yes, that's correct.

CHAIRPERSON ANASTASIO: Okay. And then my last

comment was about the modeled exposures in the NIOSH study. So one of the public comments was suggesting that the pre-1978 exposures that were modeled were lower than subsequent exposures. And they talked about this issue of the model apparently assumed a fixed calendar year, I think, of 1978 for prior years. So can you talk about exposure levels pre-1978 in terms of their magnitude compared to post-1978 and why you think this is a good approach.

DR. STEINMAUS: Yeah, exposure modeling isn't my expertise, especially when Dr. Hammond is in the room. I mean, I'll go back to the -- no exposure modeling is going to be perfect. In occupational epidemiology it's incredibly difficult to do exposure modeling. So, yes, they didn't have exposure measurements before -- I think it was actually 1976. They didn't have exposure measurements, but they had all those other pieces of data that were related -- that were directly related to exposure levels. So we're pretty sure exposures were higher before 1978 -- '76. We're pretty sure that's the case.

And it also appears that those factors that they used -- you know, again, Dr. Woods listed all of them, you know, proximity to sterilization, what they were sterilizing, you know, calendar year, all that stuff.

It's pretty clear that those factors were strongly correlated to exposure levels. So that's why I think we're pretty confident that the model was accurate.

Again, there's going to be some inaccuracies. But the question is what's the degree of those inaccuracies and what would be the impact on the relative risk that we're reported. So I did a variety of different analyses just to sort of assess. Okay, if the sensitivity exists, or if the specificity exists, or the exposure model, how would that impact the relative risks? And it wasn't going to be all that great, right? It probably wouldn't have made a huge difference to the relative risk.

So bottom line, to answer your question, yeah, we're pretty sure the exposures were higher, but we're also pretty sure that that was picked up in the Steenland exposure model.

CHAIRPERSON ANASTASIO: I see. Am I remembering wrong, that one of the public comments suggested that the OEHHA treatment -- or, sorry, not the OEHHA treatment, but the Steenland treatment this modeling of exposures was resulting in lower exposures pre-1976?

DR. STEINMAUS: I think they were saying lower than what other people might have predicted. Yeah. My understanding was the exposures were higher pre-1976.

CHAIRPERSON ANASTASIO: Okay. Okay, thank you.

Kathy.

PANEL MEMBER HAMMOND: Sure. Yeah, it's been a while since I've read some of those papers, but I did read them at one time. And Dr. Steinmaus is exactly correct that the -- what -- the effort was done on some of this was done actually at Berkeley -- UC Berkeley. They took a bunch of measurements in a lot of places. And in some places like where they put like a exhaust in, they would turn that off and do measurements. So they did measurements with all the fact -- or many of the factors that you would think would affect exposure and built a model based on that, and then retrospectively in time said when did local exhaust, for instance, come into play.

And so that's how they would develop the exposure model with all the factors that they could identify and find in the different measurements they made. So it's measurement -- a model based on measurements and with parameters that would impact exposure.

CHAIRPERSON ANASTASIO: Right. Thank you, Kathy.

Karen.

PANEL MEMBER MESSER: Yeah. Just a clarifying question. We're talking -- if someone could direct me to those comments in the public comments, that be would helpful. I think there may be some clarification that would be helpful whether we're talking about the actual

exposure being higher pre-1976 or whether the modeled exposure being too low to predict the actual exposure. So those are two different issues. If the model -- and I don't know what the comment said. From this discussion, it's hard to know what the comment -- the public comment was.

If the modeled exposure is underpredicting the actual exposure, then that would lead to bias in the eventual estimates, so that would be the issue. So it's unclear to me from this discussion whether the public comment was directed at actual exposures or a bias in the model.

CHAIRPERSON ANASTASIO: It was a bias --

DR. STEINMAUS: Yeah. Yeah.

CHAIRPERSON ANASTASIO: Yeah.

PANEL MEMBER MESSER: So do you think there is a bias in the model or -- I mean, that's always hard to --

DR. STEINMAUS: Yeah. You know, we would have no way of assessing that.

PANEL MEMBER MESSER: Right.

DR. STEINMAUS: Again, you know, we just go back to, you know, the validation data that they did have was excellent. And then, you know, they did have information available on all those factors the Dr. Hammond talked about.

PANEL MEMBER MESSER: Do their -- do their modeled exposures turn out to be higher overall pre-1976? Do you -- was there information on that?

DR. STEINMAUS: Higher than post-1976?

PANEL MEMBER MESSER: Yeah.

DR. STEINMAUS: Yeah, I'm going to have to go back and look at that, but my recollection was, yes, they were higher.

PANEL MEMBER MESSER: Okay. So that would -- that would, in a sense, be some sort of validation of the model also. Okay.

CHAIRPERSON ANASTASIO: Thank you, Karen.

Ahmad.

Ahmad, you're muted.

PANEL MEMBER BESARATINIA: Sorry about that. Yeah, just regarding Karen question, this was raised in several places in the public comment. For instance, in page 40, I think the second paragraph it was third in NIOSH exposure model based on the conditioning of calendar year predicted early sterilization and so on. So -- and they were saying that these predictions were substantially lower than workers in 1978 when exposure concentration predictions were based on measurements, so that is one thing

But the other thing, I also noticed that they are

saying that there was a loss of data -- electronic data regarding exposure estimation prior to 1978. So how could they verify this?

DR. STEINMAUS: Sorry, what's the question?

PANEL MEMBER BESARATINIA: Well --

DR. STEINMAUS: There was a loss of data.

PANEL MEMBER BESARATINIA: Yeah. They were saying that the NIOSH exposure estimation prior to 1978, the original data are lost. So how could one verify this estimation if there is no data available?

DR. STEINMAUS: Well, again, there's no -- there's no way we're going to be able to verify. There's no way we're going to be able to do, you know, a typical validation study on the exposure data before 1976, because it's just not there. So we have to --

PANEL MEMBER BESARATINIA: No. No. No. The data that they were used to make their prediction model data. So because they estimated these exposure based on some calculations.

DR. STEINMAUS: Oh, the data they used to make the model --

PANEL MEMBER BESARATINIA: Yeah.

DR. STEINMAUS: -- that they -- they said they lost.

PANEL MEMBER BESARATINIA: Yeah.

DR. STEINMAUS: Yeah, I wasn't aware of that.

PANEL MEMBER BESARATINIA: Yeah, it is indicated here in the report in the public comment section that these data are not available and they're lost. These are electronic data.

DR. STEINMAUS: Oh, I wasn't aware of that.

CHAIRPERSON ANASTASIO: Karen.

PANEL MEMBER MESSER: Yeah. I guess the answer to that is to go by the published record on how they fit the model and the model quality that they report. It seems like the underlying data may not be available for many aspects of this study, but as long as -- so that's -- I guess the point is that I don't think it puts that part of the study on any different footing, one would go by the -- their published R squared and other information on how they calibrated the model. So I'm happy to review this part in more detail from a statistical perspective.

CHAIRPERSON ANASTASIO: Yeah. I think that would be helpful.

Okay. Do we have any other comments from the Panel?

All right, seeing none, thank you very much to OEHHA for their work on this IUR.

We look forward to seeing it again. Thank you to the Panel for their comments. If you do have written

comments, you know, minor issues or even major issues, please send them to OEHHA so that they can incorporate it in the revision.

And we're now going to move to public comments.

DR. STEINMAUS: Can I make one quick comment or is it too late

CHAIRPERSON ANASTASIO: No, go ahead.

DR. STEINMAUS: You know, getting back to that exposure, I have the -- I have the exposure paper right here, Hornung. It shows the estimated levels prior to 1978 being higher than the estimated levels after 1978. That's Figure 1 on Hornung. That's the exposure paper.

CHAIRPERSON ANASTASIO: Okay. That's helpful. I think that contradicts what the public comment said about that.

Yeah. Yeah, thank you or the clarification.

Yes, Joe.

PANEL MEMBER LANDOLPH: Yeah. That curve is very interesting, you know, where you fit it and you get this shape going like that. And I'm wondering if that's two separate processes where there's really a slope with the low curve reflecting one process and the other one a different slope affecting another process. It's -- it needs a lot more thinking to go into it is what I feel. So, you know, I'd like to know more about it. We need to

know more about it. The statistical fitting looks fantastic, and -- but we --

DR. STEINMAUS: It does. Is your suggestion that we need to have a greater understanding of the mechanisms that are involved in this lower versus higher exposure?

PANEL MEMBER LANDOLPH: If that's -- if that's the case. Now, if it's one case -- if it's really, you know, a very high slope at the low dose, which is what that plot looks like, then it reminds me of some curves, you know, in metabolism where you get -- a very high slope then becomes -- something becomes saturated, binding of a molecule to receptor becomes saturated or the metabolism of, you know, a compound becomes saturated at the high dose. So I think we should try and put some more thought into it, if we could. I'll certainly try for you to help out.

DR. STEINMAUS: Yeah. I think -- I'm thinking though that ultimately it's going to be unknown. I think we can come up with some very good hypotheses, some rational hypotheses, just like what you described.

PANEL MEMBER LANDOLPH: Yeah.

DR. STEINMAUS: Maybe there's a saturation of susceptible people, so I think we can come up with some hypotheses. But ultimately, I'm not sure we're going to come up with a hundred percent answer. And I'm also

not -- I also don't -- I'm not sure that we need to come up with a hundred percent answer. But yeah, that's definitely an idea that we can put more thought into.

CHAIRPERSON ANASTASIO: Yeah, I agree fundamentally. And I think Karen said this before, you know, it's an empirical fit. So regardless of the underlying mechanism, this is the best fit to the data.

Yeah. Pam.

PANEL MEMBER LEIN: Well, that was pretty much what I was going to say, Cort. You know, I was going to push back --

CHAIRPERSON ANASTASIO: Oh, sorry.

PANEL MEMBER LEIN: -- a little bit on Joe and say I think for the purposes of risk assessment, while having a biological -- and understanding the biological mechanism certainly helps, I'm not sure it's worth the time and energy for the CARB staff to try and really dig through the literature to determine what is the reason for that kink in the curve.

For risk assessment, they don't need it and -- I did a little bit of searching, because I am a mechanistic toxicologist and there's -- what they put in the report is about what's out there for the mechanism of ethylene oxide-induced cancer.

CHAIRPERSON ANASTASIO: Yeah. Thank you, Pam.

DR. STEINMAUS: Yeah. As a scientist, it would be really cool to figure it out. As a risk assessor, you know, maybe we don't need to.

CHAIRPERSON ANASTASIO: Yeah. Karen.

Yeah. Just one last comment. I think what would be important from mechanism -- a mechanism of action perspective would be if it were biologically implausible. So I think coming up with biologically plausible mechanisms isn't super helpful here. It's just if you saw something that you thought, oh, wait, that contradicts the biology, then that might cast doubt on the model, but that is not the case here, that no one seems to feel this is biologically implausible. It's just scientific underpinning would be an interesting scientific question. So I agree with Cort that it wouldn't add to the risk assessment.

DR. KRISHNAN: And I would just add -- indicate that -- this is Krishnan -- that the application of the IUR is actually limited up to 40 micrograms per meter cubed, you know, as a result of the analysis that was indicated by EPA obviously. And EPA also had indicated that Steenland, while visiting the Cincinnati office found that the electronic data files were not available for conducting the variable approach or -- sort of follow-up somebody had indicated that.

With that, we will weave in these comments while revising our document and preparing it for SRP review moving forward, the comments we have heard.

CHAIRPERSON ANASTASIO: Great. Thank you very much, Dr. Krishnan. Thank you, Panel, for all your comments.

We're going to move now to public comment. So Arash has enabled the feature that allows participants to raise your hands. So if you are a member of the public and you would like to comment on this, please raise your hand and I will just call on you in order.

Arash, would you like to give a brief instruction on hand raising.

DR. MOHEGH: Sure. So thank you, everyone, for participating. If you are on the Zoom app, you should have either a raise-your-hand option at the bottom of your screen or you should have a reaction button where when you click that you have raise hand, lower hand option. You can raise your hand and we will start the queue. And we will basically decide how much you would allocate for the public comments based on the number of the raise hands. We also have some in-person commenters here today and some of them have submitted slides that they want to share, which I will share for them.

They have submitted them in advance and I will

share them. So let's wait a few minutes to see how many hands we're going to have and how many commenter we have and decide on the time.

CHAIRPERSON ANASTASIO: Okay. That sounds good. And in the meantime, I see that Joe is getting us off to a good start by raising his hand, so Joe why --

PANEL MEMBER LANDOLPH: No, I lowered it. I thought I lowered it.

CHAIRPERSON ANASTASIO: Oh, you lowered it. Oh. I don't have the power to do that for you.

Oh, there we go.

Arash, while we're waiting for people online to raise their hand, are people in the room set up to do their comments and share the screen?

Sorry, you're muted.

DR. MOHEGH: Yes, I have their slide right here and they're ready to share. Do you want to start with the people who are in person?

CHAIRPERSON ANASTASIO: Yeah, let's do that.

DR. MOHEGH: Okay. Let me set the slides and then have -- ask them to come to the podium. So right now, we have seven virtual attendees who raised their hand, but the number is increasing, and then we have one person in the room. So how much time do you think would be appropriate?

CHAIRPERSON ANASTASIO: Let's go for two minutes.

DR. MOHEGH: Okay. Our first commenter is Dr. Abby Li from Exponent. And let me get the slides and then get the podium for them.

(Thereupon a slide presentation).

DR. MOHEGH: Can everyone see that?

CHAIRPERSON ANASTASIO: Yes.

DR. MOHEGH: Okay. So usually, I have to share the -- basically the timer on my screen, but since I'm sharing this, then I will do the timer on my phone. And I will let you know once you are 30 seconds at the end of your time. And at the end of the two minutes, we have to cut you off.

So let me start.

CHAIRPERSON ANASTASIO: Thank you, Arash.

DR. ABBY LI: Hello.

CHAIRPERSON ANASTASIO: Hello.

DR. ABBY LI: Okay. Hi. My oral comments focus on statistical and biological considerations.

Next slide.

[SLIDE CHANGE]

DR. ABBY LI: The key issue is that the EPA IRIS model with its initial steep slope and shallower second slope -- next side, please --

[SLIDE CHANGE]

DR. ABBY LI: -- is not plausible based on the biological and epidemiological data. We're now on slide 3.

[SLIDE CHANGE]

DR. ABBY LI: EPA's rationale is based on statistical and visual fit, including the statistically significant log cumulative exposure models. This rationale is flawed because EPA incorrectly calculated the p-values, used figures for visual fit that are not fit for that purpose, and the only biological plausibility discussion was to eliminate the log cumulative exposure, because it was implausible.

[SLIDE CHANGE]

DR. ABBY LI: EPA did not include the knot as an estimated parameter in the statistics, even though it was optimized. And I'm sorry, I'm now on slide 6.

[SLIDE CHANGE]

DR. ABBY LI: Hoping you'll grant me the extra time for trying to catch up. I'm on slide 6. When corrected, as agreed to by TCEQ peer reviewers, the p-values are comparable, but the CPH model is more parsimonious.

Slide 7.

[SLIDE CHANGE]

DR. ABBY LI: Visual fit figures are misleading,

because the five dots are not the 53 individual lymphoid cancers modeled.

Next slide.

[SLIDE CHANGE]

DR. ABBY LI: Secondly, the figures give -- we're now on slide 8.

[SLIDE CHANGE]

DR. ABBY LI: -- give the appearance that models over or underestimate the grouped estimate, despite EPA's warning that making such comparisons along the Y axis should not be done.

Next slide.

[SLIDE CHANGE]

DR. ABBY LI: This misleading figures led to both errors being made in the draft IUR when concluding that models dramatically, or over, or underpredict the actual study results.

Next, slide 10.

[SLIDE CHANGE]

DR. ABBY LI: In fact, the TCEQ CPH model accurately predicts the observed number of lymphoid mortalities in the NIOSH study, and this is true overall, and locally below the not of 1,600 ppm years as well as taking into account healthy worker effect.

[SLIDE CHANGE]

DR. ABBY LI: EPA SAB emphasized any model that is to be considered reasonable must have dose response form that is both biologically plausible and consistent with the observed data.

[SLIDE CHANGE]

DR. ABBY LI: So I think I'm out of time, but my last remark is, for example, in slide 12, there is strong evidence that EtO is a mutagen. But what's important to integrate into the dose response modeling is the evidence that EtO is a week mutagen requiring high doses and long exposures.

[SLIDE CHANGE]

DR. ABBY LI: And so in slide 13, we urge OEHHA to use the standard log linear cost proportional model and the values required to derive an IUR are readily available in either the EPA IRIS or TCEQ. Thank you.

DR. MOHEGH: I'm afraid you -- Okay, thank you. Thank you, Abby, for your comments.

CHAIRPERSON ANASTASIO: Yeah. Thank you, Dr. Li.

Next commenter.

DR. MOHEGH: So we have eight commenters right now. The first person who raised their hand is Ana -- apologies if I'm mispronouncing -- Ana Kassar, I now allowed you to unmute yourself. I can't unmute you. You have to unmute yourself, Anna, if you want to present.

CHAIRPERSON ANASTASIO: Go ahead Anna. You're unmuted.

WILLIAM REMAK: Okay. Good afternoon. My name is William Remak and I'm the CEO of the California Hepatitis C Task Force. And I would like to have the opportunity -- thank you for the opportunity to speak on the agenda item number 2 on behalf of the Task Force.

And we're concerned that the updated IUR, which currently sets an acceptable risk level, that is below the levels of EtO that exist within the ambient air could unintentionally disrupt vital services within California's health care system, specifically availability of medical devices crucial for treating patients with serious conditions like hepatitis C.

We cannot afford shortages or delays in the delivery of medical services and devices, and the vast majority of which are sterilized using EtO. Such disruptions would further strain our health care system, which is already under enormous pressure. Protecting patient access should be a priority and I urge the Panel to keep them in mind as this process continues to move forward and appreciate your consideration.

Thank you.

CHAIRPERSON ANASTASIO: Thank you, Mr. Remak for your comment. We appreciate that.

Next.

DR. MOHEGH: Next, we've Richard Reiss. I'm allowing you to unmute yourself.

RICHARD REISS: Thank you.

Yes. This is Richard Reiss. I'm with Exponent and speaking on behalf of the Ethylene Oxide Sterilization Association. I'm going to focus on the TCEQ Reality Check, which was -- which has been discussed extensively so far.

There is --

DR. MOHEGH: Sorry to jump in. You had submitted some slides. Do you want them to be --

DR. RICHARD REISS: Oh, yeah. Yeah, please put them up. Yes.

DR. MOHEGH: Go ahead. Sorry.

DR. RICHARD REISS: Yeah. So -- yea, the next slide.

[SLIDE CHANGE]

DR. RICHARD REISS: So the TCEQ conducted this reality check of the lymphoid mortality predictions. And they estimated the mortalities predicted by EPA's model compared to observed mortalities. We've recast that analysis in terms of excess mortalities, which I think more clearly showed the overprediction.

And then a very important point is that EPA and

OEHHA cite TCEQ's failure to account for the healthy worker effect. However, they -- in the -- not in the draft, but in the final version of their document, they did do a sensitivity analysis related to the healthy worker effect.

So if you look on the next slide --

[SLIDE CHANGE]

DR. RICHARD REISS: -- this is the base TCEQ reality check comparing their model and EPA's model. And this is recast into excess cancers. So there are 41 excess cancers predicted by EPA's model with the central tendency and 90.7 with the upper bound. And that compares to 2.6 observed, assuming standard cancer rates of the population. So those are substantial overestimates.

Now, I understand that there's concerns that EPA didn't -- or TCEQ didn't account for a healthy worker effect, but they did do a sensitivity analysis of that. And you can see that on the next spot.

They assumed a 15 percent healthy worker effect for males and a 16 percent for females based on data in Kirkeleit. And even in that case, the EPA model, which is three and four there, overpredict the mortalities -- the excess mortalities by 337 percent and 735 percent. Not shown here, we've done that as far as 25 percent healthy worker effect and you still see an overestimate.

So I would encourage the Panel -- and as Abby mentioned, they do -- the TCEQ model itself predicts the mortalities in all, you know, in the lower dose range well. So I would encourage the Panel to go back and look at that appendix in the TCEQ assessment, and especially look at the healthy worker effect analysis that they did.

Thank you.

CHAIRPERSON ANASTASIO: Thank you, Dr. Reiss.

Next comment.

DR. MOHEGH: Our next comment is Original Dra. The Originaldra, I am allowing you to unmute yourself. You have to unmute yourself.

THE ORIGINALDRA: Okay. Thank you. So this is kind of interesting to hear you talking about this. And you know, it's important that the health care workers are not being, you know, exposed to these carcinogens. But the thing is as well is that not only when they're, you know, sterilizing devices or tools, but the masks that they've had people wear actually have ethylene oxide on -- in them, as well as the tests for the COVID tests. So even if they're just, you know, cleaning, you know, devices, they're still going to be affected if they're wearing a mask or having to be tested for COVID-19.

And FD -- the FDA actually just recently or I'm not sure exactly when, but was endorsing a new method of

sterilization that uses vaporized hydrogen peroxide. So, I mean, there are other options that can be used that aren't going to be putting people in danger like this.

But I think that if we're looking at the sterilization of that, you should also be understanding that the masks and those tests have it in them as well. That will be affecting those workers and possibly could skew your numbers, because if they're having other things come in that are exposing them to that and it's not being considered. It could possibly, you know, show that you have an influx and it just -- but from the sterilization, but you're not considering the other aspects that could bring in higher levels of that into their system as well, so it would be nice to look into that.

But I don't know if any of you have heard of the vaporized hydrogen peroxide. And that's something that you could possibly look into and -- you know, because hydrogen peroxide is also good if people are sick. So, I mean, it could do potentially the opposite, which would, you know, not cause people to be exposed to carcinogens.

And I think we need to pay attention to that with Prop 65 when people are wearing the masks and having to get tests. And that when that is required and there have been an influx in a bunch of different cancers, especially when people are stick the tests up their nose, it's

causing a lot of cancers in the brain or different areas that --

DR. MOHEGH: Dra, your time is up, if you have any closing remarks, please say them.

THE ORIGINALDRA: That's okay. Thank you.

CHAIRPERSON ANASTASIO: And thank you for comment. And I'm sorry, I didn't catch your name open.

Oh, she's back. Audra.

CHAIRPERSON ANASTASIO: Audra. Okay. Thank you for your comments, Audra.

THE ORIGINALDRA: Thank you.

CHAIRPERSON ANASTASIO: Next comment.

DR. MOHEGH: Next commenter, I'm hoping I'm pronouncing it correctly. Aracely Campa Ramirez, I'm allowing you to unmute yourself.

ARACELY CAMPA RAMIREZ: Good morning. Can you all hear me okay?

DR. MOHEGH: Yes.

ARACELY CAMPA RAMIREZ: Perfect. Thank you so much. Good morning again and thank you all for the opportunity to provide comments on OEHHA's draft cancer inhalation unit risk factor for ethylene oxide. My name is Aracely Campa Ramirez. I'm speaking on behalf of California Life Sciences and our trade partners. And we'd like to align ourselves with the comments shared by Mr.

Remak of the Hepatitis C Task Force.

The crux of our concerns stem from the unintended consequences for patients in California, especially around the issues raised pertaining to background levels. Ethylene oxide is used to sterilize approximately 50 percent of all medical devices in the U.S. each year. That's over 20 billion surgical kits, heart valves, pace makers, and is the only viable option for many devices. It does ensure stringent FDA requirements are met to meet patient safety, while ensuring effective sterilization that does not degrade the device or impact performance.

Hundreds of thousands of medical hospital and lab processes rely on these sterilized devices and equipment to protect millions of patients from the risks of infection caused by bacteria, viruses, and fungi. And any disruption in the availability of sterile medical devices and supplies could lead to delays in patient care.

Further, as others have relayed, the EPA IUR factor is lower than the naturally occurring ethylene oxide background levels currently. I believe the team at South Coast Air Quality Management District pointed out in their letter their extensive monitoring campaign to characterize ethylene oxide levels near medical sterilization facilities, as was raised by the Chair earlier, and the levels were found at these facilities to,

in fact, not be, you know, as a -- as a result of the facilities being on-site.

So, they did mention they were not aware of what sources were contributing to the background levels. So noting that the potential cancer risks at background levels alone would more than double the cancer risk from all other Pollutants and sources combined, and the significant implications this ruling would have on patients, additional information around these resources -- these sources is needed.

So we respectfully urge the Panel to take these issues into consideration, to not unnecessarily affect patients without all necessary data to adequately address the environmental concerns.

With that, I'll conclude my remarks and thank you again for the opportunity to address the Panel.

CHAIRPERSON ANASTASIO: Thank you for your comment. We appreciate it.

Next comment.

DR. MOHEGH: Next, we have Alex Khan. Alex, you can unmute yourself.

ALEX KHAN: Good morning. Can you hear me okay?

DR. MOHEGH: Yes.

CHAIRPERSON ANASTASIO: Yes.

ALEX KHAN: Thank you. Thank you for the

opportunity to speak today. My name is Alex Khan. I serve as Senior Policy Counsel for the California Chronic Care Coalition. The Chronic Care Coalition is a unique alliance of about 30 leading consumer health organizations. It includes physician and provider groups representing Californians with chronic conditions.

We really appreciate and commend the Panel's deliberative process and attention to this important issue. We'll leave the complex scientific considerations to the experts, but we do want to be here this morning to provide a patient perspective and ensure that patients have a voice.

Ethylene oxide, as has been mentioned, is one of the most common ways to sterilize medical technology. It's crucial for preventing infection in patients undergoing surgical procedures and other medical treatments. The sterilization of medical devices and instruments is critical to patient health and nearly 50 percent of all medical devices, or over 20 billion annually as was just mentioned, are sterilized using EtO.

Patients with urgent health needs cannot afford shortages or delays in the availability of needed medical devices. In many cases, it is truly a matter of life or death. We urge the Panel to consider the real-world impact on California patients and arrive at a decision

that ensures uninterrupted continuation of critical medical services.

Patients within our organization have expressed concern and we are just proud to be here and grateful for the opportunity to provide their perspective and I thank you all for the time.

CHAIRPERSON ANASTASIO: Thank you, Mr. Khan. We appreciate your comment.

Next comment.

DR. MOHEGH: Next Commenter that we have is Dr. Lucy Fraiser. Dr. Fraiser have submitted slides in advance. Let me load that.

(Thereupon a slide presentation).

DR. LUCY FRAISER: Good afternoon. Thank you. I was wondering if I could comment on the exposure model that was the subject of discussion before I get started with my planned comments. There was --

CHAIRPERSON ANASTASIO: Dr. Fraiser, you have two minutes. You can use it however you'd like.

DR. LUCY FRAISER: Okay. Well, as opposed to going -- I'm not going to talk about these slides then.

So the exposure modeling that we discussed as part of the Steenland evaluation, the -- I believe it was someone with OEHHA who referred to the Hornung study and indicated that the first figure in that study indicated

that the model predicted that exposures earlier were higher than later. But that figure that he referred to refers to concentrations from 1978 to 1986. Those are the measured concentrations. I believe that figure was just showing -- that was part of their model validation. But the exposure concentrations that are at issue are the concentrations that were modeled pre-1978 when there was no exposure data or no exposure measurements available.

And the modeling predicted that exposure levels going all the way back to the 1940s were actually lower than the measured concentrations in 1978. The data have been lost. We don't have a way to validate what's correct, but what we do know from historical experience is that that almost never happens in industry. In industry, you know, you tend to have higher concentrations early on. And then once we learn more about the toxicities, the occupation exposure levels are lowered, and the levels in the workplaces go down. So the trend that was predicted by that model doesn't make sense by comparison to what we know about other chemicals. And it also biases the inhalation unit risk estimate that EPA did, because by assuming that concentrations were lower in the early years, it significantly overestimates the carcinogenic potency of --

DR. MOHEGH: Dr. Fraiser, you are out of time.

If you have any closing remarks.

DR. LUCY FRAISER: The one other closing remark that I will make is that on our initial slide, it indicated that my comments were on behalf of the Coalition for Life Sciences. That's not correct. I was asked to do an evaluation by AdvaMed, although all the comments that I have expressed are my own.

Thank you.

CHAIRPERSON ANASTASIO: Thank you, Dr. Fraiser. Yeah, as we discussed earlier, members of OEHHA, it would be great if you could address this issue in the revised document.

Next comment.

DR. MOHEGH: Our next commenter is Jane Teta who has -- who couldn't raise their hand, but they told me that they want to give a comment.

Jane, can you unmute yourself, please?

DR. JANE TETA: I did. Can you hear me?

CHAIRPERSON ANASTASIO: Yes.

DR. MOHEGH: Yes.

DR. JANE TETA: Okay. The IRIS assessment for ethylene oxide includes a steep increasing risk at low exposures. This would imply that ethylene oxide is a potent carcinogen. Now, both the NIOSH study and the UCC study do not really support this implication. When you

look at the UCC study, it shows no increased risk in lymphoid tumors. They don't have breast cancer. We didn't have women in that study. The NIOSH study does have some positive findings, but where are they? They're in males only and they're at high -- the highest exposure categories.

In fact, females have very low risk of lymphoid tumors in that study and they have a negative trend with increasing exposure. So why do we see the pattern we see in toes dots, the categorical odds ratios, because they've combined males and females into that, the odds ratios of both together. And if you looked at 10 odds ratios and if you look maybe just at males, you might have seen a whole different pattern. So I don't believe a visual fit should be done looking at those points.

My other main issue is missing cases in the NIOSH breast cancer incidence study. Statistically significant deficit in the SMR analysis. And there is no health worker effects. Steenland says it. It's a very long follow-up study. What's the deficit? He said it. They didn't get all the cases. Okay, we understand that. That's a problem.

But the interview study is taken as a subgroup of that group. And there's more -- and then there's 32 percent who didn't participate. So now, you're missing a

huge number of breast cancer cases in the interview of study analysis, and that's what's used in the risk assessment, that data. I believe there's too much underascertainment. The mortality data is complete. The breast cancer mortality is complete. The incidence data I think is too problematic.

One other quick issue. Smoking we do not see a relationship lymphoid cancer in smokers, so many studies of smokers. The Surgeon General doesn't see it. The two studies cited by OEHHA are irrelevant. I won't go into it now, but they had the wrong disease and they had the wrong gender.

If I have any time left, I would just clarify --

DR. MOHEGH: Jane, you're out of time.

DR. JANE TETA: Okay, I'm out of time. Thank you very much for the opportunity.

CHAIRPERSON ANASTASIO: Thank you, Jane, for your comments.

Next comment.

DR. MOHEGH: Next, we have Claire Conlon. Claire, you can mute yourself.

CLAIRE CONLON: Hi. Good morning or good afternoon. I'm Claire Conlon here on behalf of Biocom California representing 1,700 companies, California research and academic institutions, medical device and

biotechnology companies. We appreciate your deliberate approach to weighing this proposal and request that you take into account the real-world impact of this adjusted factor as it relates to current FDA sterilization method requirements.

Biocom California aligns our comments with the patient groups focused on the large-scale need for sterilized medical devices and the limitation of sterilization services without a workable alternative ready to replace the existing sterilization capacity could jeopardize access to medical services ranging from preventative care to critical surgeries. So we urge OEHHA to leverage your own expertise and revise the draft IUR to protect public health.

Thank you.

CHAIRPERSON ANASTASIO: Thank you, Claire.

Next comment.

DR. MOHEGH: Next, we have Keya Gupta. Keya, you can unmute yourself now.

KEYA GUPTA: Good morning. Can you all hear me?

DR. MOHEGH: Yes.

KEYA GUPTA: Wonderful. Thank you for the opportunity to be here today and comment on agenda item number 2. I do work in health care.

As you assess the updated risk factor for

ethylene oxide, I would urge the panel to recognize the irreplaceable role that EtO plays in the sterilization of numerous medical devices, as many of devices cannot be sterilized safely without any -- with any other proven methods.

I believe that we should do everything in our power to avoid a disruption in the supply chain of critical medical tools, which would intern severely hinder the delivery of essential health care services from life saving surgical procedures to routine preventative care, and could potentially compromise patient safety across the state of California and beyond.

Additionally, it's crucial to evaluate the validity of the research, particularly considering it is predicated on an EPA assessment dating back to 2016. California's health care system is already navigating very formidable challenges, including workforce shortages. And in this context it is paramount that regulatory decisions do not exacerbate these struggles by constraining access to vital medical equipment.

Thank you for your time and for considering the insights that all participants are offering today. Appreciate it. Thank you

CHAIRPERSON ANASTASIO: Thank you, Keya, for your comment.

Next comment.

DR. MOHEGH: We don't have anyone else currently raising their hand. I do see one phone call-in listener. If they want to give comments, they can press star nine on their phone and raise their hand. If not, I don't see any more hand raised.

CHAIRPERSON ANASTASIO: Great. I'd like to thank everyone who gave a comment. And I see that Kathy has her here raised. So, Kathy.

PANEL MEMBER HAMMOND: I would like to thank the commenters as well and just make a general comment. They're -- to remind people, this came up earlier, that there are two steps in this process. One is to evaluate how risky a chemical is, and then if it's risky, there's another step for managing that risk. And the management of the risk is actually where these issues and the trade-offs will come into play. So you don't want the people who are managing the risk to be using inappropriate risk assessment. So we need to have good -- the best estimates of what the risks are for the chemicals. And then that information can go into trying to figure out how to control those risks. And it may be controlling the exposures. It might be a question of making sure there are more controls to the exposure not eliminating something.

But that is the next step that's outside of this Science Review Panel. Our goal is just to get the best estimate of the risk and to evaluate that based on OEHHA's work.

CHAIRPERSON ANASTASIO: Yeah, that's a very good point, Kathy. Thank you for that. Right, we are not considering risk management aspects of EtO. That would be a secondary -- or a second process.

Okay. Well, thank you, everyone. Thank you to OEHHA for the presentation. Thank you to the Panel for your comments, and then also thanks to the public for their comments.

We're going to move on now to our next agenda item, which is informational update on the Community Air Protection Program. The California Air Resources Board staff from the Office of Community Air Protection, OCAP, are going to update us on Blueprint 2.0, which is the updated statewide strategy to reduce exposure in communities most impacted by air pollution. We, as the Panel, are one of several groups that CARB has regularly consulted with about the implementation of this program.

On October 26th 2023, the CARB Board approved Blueprint 2.0, which includes goals and action items, and renews CARB and air district commitments to implement the strategies in the community emission reduction programs

approved by the Board.

Significantly, Blueprint 2.0 provides new pathways to support communities that have been consistently nominated for the program. CARB staff will also provide a brief update on the recent award of $10 million to a total of 24 -- or sorry, 42 tribal and community-based organizations throughout the state and their plans to conduct third-party programmatic evaluation of program as committed to in the Blueprint.

So I am now going to introduce Dr. Brian Moore, who's the Supervisor of Community Planning Section from CARB to give us this informational item. And thank you, Brian, for coming to speak to us.

(Thereupon a slide presentation).

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

Great. No. Thank you all. I hope you can see my slides okay right now and hear me all right.

CHAIRPERSON ANASTASIO: Yes.

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

Oh, great. Great. So again, I am Brian Moore and I'm a manager in the Office of Community Air Protection. And we are responsible for the implementation of Assembly Bill 617 and the Community Air Protection Program. It's really nice to see you all again and I am excited to update you on the latest progress that we've

made since the last update as well as our plans moving forward.

And just quickly before I start, I just wanted to point out the relevance of the SRP activities to the Community Air Protection Program. We work in some communities in Southern California that are home to a lot of these sterilization facilities that use ethylene oxide. So that's just a -- you know, one example of the direct connection between the work you all are doing and, you know, how we implement things, you know, on the ground in these communities.

[SLIDE CHANGE]

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

And so this slide here is just a brief outline of this update. I did want to share the new direction for the program now that we have those revised -- everybody's guide document, the Blueprint 2.0 that has been approved by our Board. And I wanted to highlight three new components of that program to help us moving forward, and then kind of end with just focusing on some priority actions for this next year specifically.

[SLIDE CHANGE]

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

And again, our statewide strategy was approved unanimously from the CARB Board in October. And I --

here, I just wanted to revisit the figure that kind of illustrates the structure of this -- of this document -- this guidance document.

So on the left side, we illustrate part one in that green. And it's a five-year strategic plan centered on civil rights, environmental justice, and Equity principles. This plan is based on guiding principles that were developed from lessons learned over the first five years of the program. And an example of this would be our priority to support power sharing between community members and agencies. We did notice that stronger collaborations definitely led to more successful plan development. And this happened when public agencies became willing to create some space for community direction whenever possible as these plans are being developed.

So on the right side of the screen, in the blue, we have our part two, which is our implementation guidance. And that implementation guidance is really split into two parts. So on that left side of the blue, we really want to emphasize that we are committed to successfully implementing the 19 current community emissions reduction programs that are in involvement. So we have 19 communities that are kind of in the process of our traditional way of developing plans. And so we really

want to see those through and really focus on tracking of progress and accountability within those plans, which we call CERPs.

And then on the right side of the blue, this is our new implementation strategy. And so this focuses on outreach and action in the communities that have been consistently nominated, but have not yet been selected for that traditional community emissions reduction program or CERP development.

And with this new strategy of three pathways to accomplish this, the first, we want to take those communities air grants that were mentioned that were awarded to the community-based organizations to fund the development of local plans, which we are calling L-CERPs this moment. So that's one way.

Another way we want to implement the strategy is to increase the way air districts and communities can use our community air protection incentive funds by revising their guidelines to make them a little more flexible.

And then the third way is CARB enforcement -- our Enforcement Division is partnering with a lot of communities to implement community-focused enforcement efforts.

[SLIDE CHANGE]

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

So this slide kind of represents one of those new pathways that I mentioned, the community air grants. So these grants are designed to provide resources to support community-based non-profit organizations and tribal governments in the push for cleaner air in their communities. And this slide here describes the latest round of the community air grants that were awarded and kind of the three major types we see. So if you look at that pie chart, we had educational grants awarded, as well as technical ones, which this includes like any citizen science or community led air monitoring. And then we also had some targeted projects approved. And this include that idea to fund these local plans, these L-CERPs that I mentioned earlier, you know, that are part of one our new pathways.

So eight of these targeted awards to create these local plans were awarded this year. And, in general, 18 of these 42 projects that were awarded are based in our consistently nominated communities. So those are those communities we want to reach out to. So we see this as a way that we can direct resources into those communities really quickly and start building capacity. And I guess just to kind of finishing things off with the community air grants, we are actually having another round of solicitations for the next cycle of grants. That would be

our fifth year and that is coming up this year.

[SLIDE CHANGE]

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE: So now, I'll focus on our community air protection incentive program. So these are -- this program is statewide and these incentive funds are -- can be used in disadvantaged and low-income communities across the state. And they're implemented by the air districts, but based on CARB guidance. So the CARB guidelines currently provide criteria and guidance for air districts to implement a wide variety of different project categories, which we would call chapters, because each one is a chapter in this guideline document. And we intend to update some of the existing categories add new ones.

So over the past three years, air districts and communities have taken advantage of this community identified project pathway and created a dozen new kinds of projects for these selected communities that are developed during a traditional CERP. So these are -- these are projects that the community got together with the air districts to develop guidelines for that CARB had not. And then we at CARB look at those guidelines and then either tweak them or approve them based on, you know, funding guidelines.

So the idea is that we want to take the more

popular and successful of these community identified projects and make them available statewide by creating new projects and chapters that are just available to use right off the shelf. So no new communities will have to go through that process of starting from scratch to develop these projects. And that's what's shown kind of on the right side of this figure in the blue. And so these are examples of those new chapters and new projects that will ready to go, stuff like agency partnerships to work on truck rerouting, vegetative barriers, urban greening, paving projects. We just had a groundbreaking of a paving project in Heber in Imperial County. Bike paths and sidewalk installation. And then also ag burning alternatives and like incentivizing low dust nut harvesters in ag communities. So these are all new chapters that will be added to the guidelines.

[SLIDE CHANGE]

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

This slide just indicates the timeline for the community air protection incentive guidelines revisions. Air districts requested a longer public process, so we did expand our timeline to work on our guideline revision -- revisions in collaboration with the air districts and community members. So we've seen more discussions we've had with the various air districts. And actually this

week right now our incentive team with the air district incentives staff are participating in a retreat to go over the draft guidelines. And then also, we're hoping in April, we will finalize the incentive -- new incentive guidelines and after workshopping the draft guidelines with the public.

[SLIDE CHANGE]

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE: And just to kind of end up, I wanted to panned out to the bigger picture of the program. So looking at the goals moving forward for the program, you know, with our five-year strategic plan, it really focuses on these eight goals here presented on this slide. And some of these goals carry over from themes in the original blueprint, such as the emphasis on partnering and using regulatory authorities at CARB and the air districts. And really related to this, you can see that the -- I want to note goal 4 in the top right corner that -- which speaks to working on both mobile and stationary sources at CARB and with air district collaborations.

Lessons learned from the -- from the first five years of the program and our extensive engagement helps shape and refine these goals, such as making sure it is centered work in -- our work in civil rights, equity, and environmental justice. Other new goals reflect the

reality that in the next five years of the program, we must focus on communities that have been consistently nominated for the program, but not selected. So our kind of historical pattern of only being able to select, you know, two, to three, to four communities for CERP development just isn't going to get it done. We need to be able to roll out benefits and resources faster to more communities.

So with that, each goal area includes actions that we've committed to.

Oop. Sorry.

I'm sorry. Unless, Arash, you intentionally shut me down.

DR. MOHEGH: I did not.

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE: I think -- I think my arm hit my space bar. Sorry about that. I know everyone wants -- okay. So let's see. Let me do this again.

Awesome. Wait. Here we go. Did that pop back up okay?

DR. MOHEGH: Yes.

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

Oh, okay, great. Here we are.

And so sorry about that interruption, but as I was mentioning that we have these kind of not lofty but

larger umbrella goals. And for each of these we have developed some key actions to implement these goals. And I wanted to share just a few that are priorities for this upcoming calendar year for 2024.

[SLIDE CHANGE]

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE: So here's some of those key actions that we'll be working on this year to hopefully push us towards achieving the five-year strategic plan. So the first one is a programmatic evaluation from a third party. We have seen with other similar programs, like the transformative climate communities work over at the Strategic Growth Council. They've really benefited from these third-party evals. So that's something we are doing this year.

Another action is the standardized and required training environmental justice, public participation, and civil rights for all our staff and management at CARB that worked on Assembly Bill 617.

And we are also prioritizing developing engagement strategies for the 60 plus consistently nominated communities that we have identified over the five years. So it's been a long process creating this list, so we need to start our outreach as soon as possible with these communities.

And as we -- I already mentioned, we do want to

complete the revision of our community air protection and incentive guidelines to create more flexibility and streamline the process. And as well, we want to provide training and support for future community air grant recipients. They're trying to develop those local plans, those L-CERPs. We actually have a pilot one going on now. And we're learning a ton about how those could be successful with this pilot. So hopefully moving forward, we can really support these community-based organizations that receive these grants to develop their own plans.

And finally, the last one is a little more practical one, but our goal is to redesign our web presence so it is more accessible and really reflects the revised guidance of Blueprint 2.0, because it's getting a little dated, so we do want to make sure that we get all the tools, resources, and information on the program up to date and available as soon as we can.

[SLIDE CHANGE]

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE: And with that, that is -- that is the end of my update. If anyone has any questions or concerns, I'm more than happy to answer them. And can you always give me a call or email us or go through Arash to get in touch with me if anything comes up in the future. So thank you.

CHAIRPERSON ANASTASIO: Great. Thanks very much

Brian.

Are there comments or questions from the Panel?

Ahmad.

PANEL MEMBER BESARATINIA: Thank you, Cort. Thank you, Brian, for the update.

I was just wondering in one of your slides you mentioned that you are approaching the solicitation phase for grant proposal. And I'm wondering do you inform the potential applicants about your priority areas? Do they know what are the priorities when they apply? Is there a website or are there other mechanisms in place?

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

Yes. Just to clarify, you mean like priority geographic areas, not like whether it's a technical, educational, or targeted grant.

PANEL MEMBER BESARATINIA: (Nods. Head)

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

Oh, yeah, so we do. And I can share that with the group. We have a -- we have a list of these 65 plus communities that we really want to focus on and then we also have kind of the methodology for how we -- how we came up with developing this list. It was, I'd say, semi-quantitative effort. You know, we didn't just want to rely on the -- developing one like ubermetric that could, you know, misclassify things or could be biased.

So we really based it on a lot of the community input we've received, air district capacity. So it was a -- yeah, it was a -- quite a process to develop that list. And it is posted.

And our plan is -- you know, we have this list for this first year, but we plan over the next few years, not maybe this first year, is to really reach out to other communities to add to that list, so it's not a static list. And we'll be updating it at regular intervals moving forward. And I'll share that list with Arash, so that you all can check it out.

PANEL MEMBER BESARATINIA: Thank you very much.

CHAIRPERSON ANASTASIO: Great. Other questions or comments.

So Brian, if I caught it correctly, you have an increase in budget for the community programs in the coming year?

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

Oh, yeah, so -- and I want to make sure I have that right, so that the community air grants they've kind of been staggered, and with COVID where we sometimes have combined budget years into one solicitation, so I don't want to say yes. But I guess, yeah, we should have close to 16 million, which is more than the last cycle offered, but maybe due to like combining years of allocations from

the Legislature, right, because we were -- we have setbacks. So I'm not positive if that's due to a legislative increase. I can't remember off the top of my head or if it's due to kind of the word staggering of when the grant cycle comes around versus legislative funding.

CHAIRPERSON ANASTASIO: Gotcha. Okay. Well, I'm hoping for a legislative increase, but --

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

Oh, we were -- I do want to say like we were really supportive of this latest round of budget cuts so far that the Legislature and community have been really supportive. And so we've been able to -- and not to see some of the cuts of some other programs, you know, across the state. Yeah.

CHAIRPERSON ANASTASIO: That's great.

Okay. Well, thank you again, Brian and than you, Panel. I'm now going to open it to public comments. So, as Arash mentioned, you should -- if you're connecting via Zoom, you should be able to use the raise-hand function on the lower right-hand side of your Zoom screen. And if you raise your hand, we'll call on you and you'll have two minutes to make your comment.

DR. MOHEGH: Okay. I can see two people who have raised their hand.

CHAIRPERSON ANASTASIO: Okay, fantastic. Let's

start and maybe other people will join in.

DR. MOHEGH: Okay. Our first commenter, and apologies if I'm mispronouncing, Kathy Kerridge. You can unmute yourself, if you want to provide oral comment.

KATHY KERRIDGE: Hi. Thank you. And thanks for the presentation. And you did get my last name right, so congratulations.

I have more of a question than a comment. I live in Benicia. This is -- we are a refinery community, but we are not an EJ community. And I think that I've nominated our community maybe in the past. I'm not quite sure. But is there any hope that communities that have large stationary sources -- I mean, we're by EJ communities but not ourselves. Is there any hope that we can ever get any of these community grants. Right now, we do run an independent air monitoring station through the Benicia Community Air Monitoring Program, but we have limited funds for that. So, you know, in the future, we may not be able to run it any more. So just -- I've just got a question about accessibility of any of these grants for non-EJ communities.

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

Yeah, real quick, Kathy. I hope -- let me -- I'll put my email -- I don't know if I can chat you my email. But I guess the short answer is yes, there are

mechanisms to supply funding for even, like you mentioned, like a community air monitoring network. And we do -- some of our current communities that we're trying to develop strategies for, Richmond is one that we're working in that's by you, and then also down south in some of the refinery communities. So part of this program is trying to attack the issues with stationary sources, even those larger ones.

So yeah, if there's a way, I'll get you my contact information and I can introduce you to our community air grant staff and talk about ways that hopefully we can get some resources to you.

KATHY KERRIDGE: Okay. That would be great. Yeah, I think I got your email. It's -- is it brian.moore@arb.ca.gov?

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

Yep, it's in the presentation. And then some of these -- I mentioned disadvantaged communities, but some of these incentive funds and CAGs can be spent in other locations. Now, the majority we try to spend -- and the law compels us to spend them in disadvantaged communities, but there are other pathways. Yeah.

KATHY KERRIDGE: Okay. Great. I will be emailing you. Thank you.

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE:

Sounds good.

CHAIRPERSON ANASTASIO: Thank you.

DR. MOHEGH: Thank you, Kathy. Brian, if you'd like, I can put your email and contact information in the chat.

KATHY KERRIDGE: Oh, that would be great. That would be great.

CHAIRPERSON ANASTASIO: Our next commenter is The Originaldra. Dra, you can unmute yourself.

CHAIRPERSON ANASTASIO: So Audra, before you start, can you give us your full name?

THE ORIGINALDRA: Sure. Audra Morgan.

CHAIRPERSON ANASTASIO: Thank you.

THE ORIGINALDRA: Um-hmm.

CHAIRPERSON ANASTASIO: What is your comment?

THE ORIGINALDRA: Well, my comment is that, you know, as we sit here and incentivize different things, you know, the County of San Diego, SANDAG, for their 2025 regional plan wanted to do a vehicle miles traveled for the community and charge us to travel per mile. And, you know, I know that they took that away, because, you know, the people weren't happy with it, but it's still coming down the pike from the state, that that's going to be something that's implemented.

But with all of the regulations if -- you know,

the problem is is that all of these things are pushing us into not walking -- I mean, not driving, and walking, or biking, or using public transit. And if the plan doesn't, you know, encourage just that, then a lot of times we don't get funds for things that we need in the community. And it's sad to see that, you know, like they will demonize driving and say, you know, all of these crazy things to the people when a lot of this stuff is -- like everything that we're doing for the green energy is totally toxic to the environment, and to people, and when you're mining for it.

So I mean, I don't understand why we can't look at those things when you're talking about, you know, air pollution, and, you know, the public health and safety of people. But then we do things like engage in stuff that's toxic to the environment, and also again the people's health, because all of this green energy, I mean, it emits radiation when you're using it, first of all when it's made. But just to make all of these -- this technology, it will never save as much greenhouse gas as it produces while it's being made and manufactured.

And so it's almost as if like we can acknowledge some things and not others, because this like -- it has become the climate God. And people are willing to sacrifice anything to this God. It doesn't matter if it

costs us more money and we'll put us -- everybody in debt just to push this agenda. It's really hard when, you know, there's things that it's causing that nobody wants to acknowledge. And it's blatantly ignored, because there's a bigger picture into this and it's just -- I just don't understand how you guys can work on things like that, and then --

DR. MOHEGH: Dra, you're at the end of your allocated time. If you have any closing remarks, please --

THE ORIGINALDRA: Yeah. I just would like to know why it's being ignored when we're saying that we care about those things. I would just hope that you could acknowledge that. And even the chem trails that are above us that affect the weather that affect the air. So it would behoove you to look into it.

CHAIRPERSON ANASTASIO: All right. Thank you, Audra, for your comments.

Are there any more public comments, Arash?

DR. MOHEGH: There is no more.

CHAIRPERSON ANASTASIO: Okay. Then we will close public comments.

And any further comments from the Panel on either of our items, EtO or the Blueprint 2.0?

All right, if not, we'll move on to our final

item, which is consideration of administrative matters. So, we are hoping to have our next meeting in June. As I mentioned at the beginning of this meeting, Paul Blanc, Kathy Hammond, and Mike Kleinman are all rotating off the Panel. I'd like to thank all three of them for their years of service. I'd also like to thank them for -- well, Kathy, for attending this meeting. We really appreciate your input, Kathy.

Just to note, two Panel members, your term may end, but you can actually serve until there's a replacement named for you. And the replacement naming process sometimes is a little slow. So Kathy, if we don't have a new person for you by June, I hope you might join us.

Oh, wait, and Beate is also ending? Is that true, Beate?

So Beate, you ended December '23 or is it going to December '24?

PANEL MEMBER RITZ: No, '23, but I was asked, since there's no replacement, to be participating until somebody is nominated.

CHAIRPERSON ANASTASIO: Oh, okay. I didn't realize that are also. Well, thank you for your many years of service as well. So I hope that retiring members will continue to serve until we have new members, because

otherwise quorum is very difficult and we appreciate your input.

One other item might. Mike was the SRP Community Liaison. So with his stepping off the Panel, we need a new liaison. I was going to ask him at this meeting what the liaison entailed. But since he's not here, I'll do that over email and then I'll send it out to the Panel in the hopes of finding a new liaison from the Panel to OCAP items.

Okay. And that is all I have on my list. Are there any final thoughts?

It looks we're all good.

All right. Well, I appreciate everybody coming today and spending the time. And I hope you have a great rest of your day and a great weekend.

DR. MOHEGH: How much -- I just want to mention that you can find all the materials available on our website for this event, which I just posted and I have been posting throughout the meeting. You can find the slides that are shared. I will make available the recording and the transcripts that will be available in the next few weeks. And we will also make available the slides that people have shared unless they object to it. So everything will be made available publicly

CHAIRPERSON ANASTASIO: No, that's great.

Well, thanks to OEHHA and CARB for the presentations. Arash, thank you for being the man behind the scenes, even though it looked like you cut Brian off there for a second.

OCAP COMMUNITY PLANNING SECTION MANAGER MOORE: No, that was totally my fault. I confirmed that was user error. I didn't mean to blame Arash. That was me.

(Laughter).

CHAIRPERSON ANASTASIO: We're going to think now about giving Arash real power over any speaker to mute and stop you from saying anything further. That will be under consideration at our next meeting.

And I think that's it. The meeting is now adjourned and have a great weekend, everyone.

(Thereupon the California Air Resources Board, Scientific Review Panel adjourned at 12:37 p.m.)

CERTIFICATE OF REPORTER

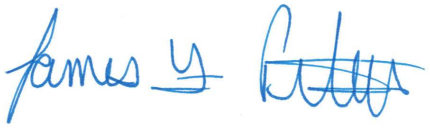
I, JAMES F. PETERS, a Certified Shorthand Reporter of the State of California, do hereby certify:

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 18th day of February, 2024.



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