MEETING

STATE OF CALIFORNIA

ENVIRONMENTAL PROTECTION AGENCY

AIR RESOURCES BOARD

SCIENTIFIC REVIEW PANEL

ON TOXIC AIR CONTAMINANTS

ZOOM PLATFORM

CALEPA HEADQUARTERS

1001 I STREET

SACRAMENTO, CALIFORNIA

THURSDAY, FEBRUARY 13, 2025

9:32 A.M.

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

J&K COURT REPORTING, LLC

APPEARANCES

PANEL MEMBERS:

Cort Anastasio, PhD, Chairperson

Ahmad Besaratinia, PhD

Paul Blanc, MD

Katharine Hammond, PhD

Michael Kleinman, PhD

Joseph R. Landolph, Jr., PhD

Pamela Lein, PhD

Karen Messer, PhD

Beate R. Ritz, MD, PhD, MPH

REPRESENTING THE AIR RESOURCES BOARD:

Hnin Hnin Aung MsC, PhD, Air Pollution Specialist, Health and Exposure Assessment Branch, Research Division

Arash Mohegh, PhD, Health and Ecosystems Assessment Section, Health and Exposure Assessment Branch, Research Division

REPRESENTING THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT:

Kannan Krishnan, PhD, Assistant Deputy Director, 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

Meng, Sun, PhD, Chief, Air and Site Assessment and Climate Indicators Branch, Division of Scientific Programs

APPEARANCES CONTINUED

REPRESENTING THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT:

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

ALSO PRESENT:

Byanka Santoyo, Center on Race, Poverty and the Environment

INDEX

INDEX CONTINUED

PROCEEDINGS

CHAIR ANASTASIO: Good morning, everyone. And I'd like to call this meeting of the Scientific Review Panel on toxic air contaminants to order. Welcome, everyone who's coming from online. Please note that the meeting is being recorded.

Hnin Hnin Aung will be overseeing the Zoom technical operations and she's going to go over instructions for comments once we get to public comments. We're going to start with Panel introductions. But before I get to that, just a note, we are well aware that many of the Panelists, including myself, our terms have ended, either last year, or even before that. Fortunately, everyone is allowed to serve until a replacement is seated. And I just want to say we really appreciate everyone participating, especially those members whose terms have ended. I promise this is not a life-long appointment. There will be replacements. I just don't know when.

So now let's do Panel introductions. I'll start. I'm Cort Anastasio. I'm Chair of the Panel and I'm a professor of at UC Davis.

Paul.

Sorry, Paul, you're muted.

PANEL MEMBER BLANC: Paul Blanc, Professor

Emeritus, University of California, San Francisco. Panel member for occupational health.

CHAIR ANASTASIO: Thank you, Paul.

Kathy.

PANEL MEMBER HAMMOND: Kathy Hammond, Professor Emeritus, UC Berkeley and professor of the graduate school there, and a member of the Science Review Panel.

CHAIR ANASTASIO: Thank you, Kathy.

Beate.

PANEL MEMBER RITZ: Beate Ritz, Distinguished Professor of epidemiology and environmental health, COEH member at UCLA, School Public -- School of Public Health, I am one of those expired members still here.

(Laughter).

CHAIR ANASTASIO: Not expired.

PANEL MEMBER RITZ: Yeah, well, expiration date passed.

CHAIR ANASTASIO: You still have plenty of shelf life.

(Laughter).

CHAIR ANASTASIO: Thank you, Beate.

Mike.

PANEL MEMBER KLEINMAN: I'm Mike Kleinman. I'm a Professor at UC Irving. I'm an inhalation toxicologist and I am also on the list for expiration.

(Laughter).

CHAIR ANASTASIO: Thank you, Mike.

Pam.

PANEL MEMBER LEIN: Hi. I'm Pam Lein, Professor of neurotoxicology at University of California, Davis School of Veterinary Medicine. And like everyone else, I'm expired as well.

CHAIR ANASTASIO: Thank you, Pam.

Ahmad.

PANEL MEMBER BESARATINIA: Good morning, everybody. Ahmad Besaratinia. I'm a professor of at Keck School of Medicine of University of Southern California, los Angeles.

CHAIR ANASTASIO: Great. Thank you, Ahmad.

And then last, Joe.

PANEL MEMBER LANDOLPH: Hi. I'm Joseph R. Landolph, Jr., PhD. I'm Associate Professor of molecular Microbiology and immunology and associate professor of molecular pharmacology toxicology in the Keck School of Medicine. And I work on molecular carcinogenesis and genetic toxicology at the Keck School of Medicine of the University of Southern California.

Thank you

CHAIR ANASTASIO: Great. Thank you, Joe, and thank you all, Panelists.

First, an overview of the meeting today. We have just one item from OEHHA, which is a reference exposure level, affectionately called a REL., for 1,4-dichlorobenzene. We were -- we will take public oral comments on this item after the presentation and then the Panel discussion.

So, let's get into that. So staff from the Office of Environmental Health Hazard Assessment, OEHHA, will present a draft document with an update of reference exposure levels, RELs, for 1,4-dichlorobenzene. RELs, to remind everyone, are airborne concentrations of a chemical that are not anticipated to result in adverse non-cancer health effects for specified exposure durations in the general population, including sensitive subpopulations.

OEHHA is required to develop guidelines for conducting health risk assessments under the Air Toxic Hotspots Program, Health and Safety Code section 44360(b)(2). In response to the statutory requirement, OEHHA developed draft RELs for 1,4-dichlorobenzene. Workshops and comment period for the document were offered from November 2024 through January 2025. More information regarding the document can be found at a URL that I hope Hnin Hnin will put into chat, so I don't have to say the whole thing.

And I would like to now introduce Dr. Rima Woods,

Senior Toxicologist and one of the item leads from OEHHA.

Rima, the floor is yours.

(Slide presentation).

DR. RIMA WOODS: Thank you very much, Cort. I will share my screen. Okay. And I just want to confirm that you can see my screen okay -- see my slides.

Great.

Okay. Good morning everyone. Dr. Rima Woods, Senior Toxicologist and Chief of the Air Toxicology and Risk Assessment section at OEHHA. I'm joined today by Dr. Meng Sun, Chief of the Air and Site Assessment and Climate Indicators Branch, Dr. Rona Silva, staff toxicologist in the Air Toxicology and Risk Assessment Section, and Dr. Kannan Krishnan, Assistant Deputy Director of Scientific Programs for OEHHA.

Today, I'll be presenting the derivation for draft acute eight-hour and chronic reference exposure levels for 1,4-dichlorobenzene. And if approved, these RELs will be adopted into the Air Toxics Hot Spots Program.

[SLIDE CHANGE]

DR. RIMA WOODS: Okay. This is the structure of 1,4-dichlorobenzene, or 1,4-DCB, with chlorines on opposing sides of a benzene ring. 1,4-DCB is often referred to as para-dichlorobenzene. So, it's a solid at

room temperature, but sublimes going from solid to gas relatively easily. This characteristic led to it's use in air fresheners and as an insect repellent in mothballs. 1,4-DCB has a melting point of 52.7 degrees Celsius, or 127 degrees Fahrenheit, and it has a vapor pressure of 1.74 millimeter mercury, or Torr. It is soluble in many organic solvents, but is insoluble in water.

[SLIDE CHANGE]

DR. RIMA WOODS: The main use of 1,4-DCB in California is as an active ingredient in mothballs and is also used as a pesticide in residential and commercial spaces. It's been banned in California for use in air fresheners. Other uses are as a component in the manufacture of polyphenylene sulfide thermoplastics, which are used in the electronics, automotive, and aerospace industries. 1,4-DCB can be found in some oil or fuel additives and construction products. Main emission sources in California are sawmills and lumber producers, water treatment facilities, and some landfills. It is listed as a carcinogen under the California Proposition 65 program and has an inhalation unit risk factor under the Hot Spots Program.

Today, we're presenting an updated chronic REL, which will supersede the current chronic REL of 800 micrograms per cubic meter, or 133 ppb, which was based on

liver hypertrophy in rodents. U.S. EPA's IRIS program developed this value in 1994, and OEHHA adopted it into the Hot Spots program in 2000.

[SLIDE CHANGE]

DR. RIMA WOODS: But monitoring efforts have evaluated airborne concentrations of 1,4-DCB. A study of residents in the Los Angeles area in 1987 found detectable levels in 59 percent of exhaled breath and 77 percent of personal air samples, which was likely associated with indoor use air fresheners and mothballs.

For ambient air levels, the California Air Resources Board collected air monitoring data for 1,4-DCB in urban areas from 1990 up until 2007. The maximum level of 1,4-DCB in any one year during that time ranged from 0.4 to 3.1 parts per billion. However, in most measurements, 1,4-DCB was below the limit of detection.

[SLIDE CHANGE]

DR. RIMA WOODS: 1,4-DCB is rapidly absorbed via inhalation and oral routes, but not through dermal routes. In inhalation studies performed in rats, 1,4-DCB distributed to fat, but declined to low levels by 24 hours post-exposure, suggesting that 1,4-DCB does not have long-term storage in the fat. It also distributes to a lower extent to liver, kidney, and serum.

The primary route of metabolism for 1,4-DCB is

via oxidation by cytochrome P450s in both rodents and humans, primarily to 2,5-dichlorophenol, or 2,5-DCP.

CYP2E1 is the main isozyme involved in metabolism. 2,5-DCP is conjugated to glutathione and eliminated in urine. In the only controlled inhalation study in humans, by Yoshida et al., 2002a, between five and 16 percent of the absorbed 1,4-DCB was eliminated in urine as 2,5-DCP at nine to 11 hours after exposure began. However, the study only lasted about 10 hours following the end of exposure, so the authors were not able to determine a urinary elimination half-life in humans.

[SLIDE CHANGE]

DR. RIMA WOODS: Since the 1980s, NHANES has been collecting urine samples from adults and children during their periodic population surveys. Urinary levels of 2,5-DCP are included in the survey and this is considered a reliable biomarker of previous exposure to 1,4-DCB.

The surveys found detectable levels of 2,5-DCP in 98.5 percent of urine samples in the 2007-2008 and 2009-2010 survey cycles, showing that non-occupational exposure to 1,4-DCB is widespread. However, levels have been declining since the 1980s. For example, as shown in this table, the 50th percentile for 2,5-DCP in urine has dropped from 24 micrograms per gram creatinine in the '88-'94 survey down to 2.03 micrograms per gram creatinine

in the 2015-2016 survey.

[SLIDE CHANGE]

DR. RIMA WOODS: I'll now turn to the acute toxicology data for 1,4-DCB, which was assessed to derive the acute REL. There is very limited information on acute 1,4-DCB exposures in humans with durations of 24 hours or less. There are early occupational health studies from the 1950s, which suggests that sensory irritation can occur at concentrations of 50 to 80 parts per million.

However, the methodology used to determine the air concentrations was not well documented and a clear quantitative correlation between concentration and the sensory irritant effects could not be determined. In animal studies, a concentration of 70 -- 798 ppm for eight hours daily resulted in tremors, weakness, and eye irritation. It was unclear from the study if the first day of exposure resulted in these effects, or if multiple daily exposures were needed to cause the effects.

In a more recent two-generational study by Tyl and Neeper-Bradley, a concentration of 571 ppm on the first day of a multi-day exposure resulted in tremors and sensory irritation in male and female rats. Umemura et al. exposed male rats to concentrations of 125 or 500 ppm for 24 hours, which caused microscrap -- excuse me, microscopic cellular damage to the kidneys, including

epithelial swelling, eosinophilic bodies, and desquamation in the kidney proximal tubules. In female rats, exposure to 500 ppm for 24 hours showed vacuolization in hepatocytes.

[SLIDE CHANGE]

DR. RIMA WOODS: Now, I'd like to describe the chronic and subchronic effects of 1,4-DCB exposure in humans.

Evidence of chronic injury has been mainly through case reports and reviews of exposure to 1,4-DCB, primarily via the inhalation route, but also via the oral route. Exposure was on the order of months to years in these case reports. Very early case reports from the 1950's documented liver damage while newer studies documented central nervous system toxicity and dermatitis.

The main finding of more recent case studies involving substance addiction was nonspecific damage to white matter of the brain, known as leukoencephalopathy, leading to functional neurological decline. Symptoms include limb weakness, tremor, bradyphrenia, which is slowed thinking and processing of information, and cognitive decline. Leukoencephalopathy can be caused by a variety of different agents, including exposure to other types of environmental and industrial chemicals.

Dermatitis was also a common finding in these

cases, but evidence of liver or kidney damage was not. Exposure to 1,4-DCB was confirmed by the presence of 2,5-DCP in urine, or 1,4-DCB in blood. However, it is possible that exposure to other chemical substances could have occurred but was not confirmed in these reports.

[SLIDE CHANGE]

DR. RIMA WOODS: And there are a few occupational studies available for 1,4-DCB. In the occupational health study by Hollingsworth in 1956, spot air samples collected from various locations within the workplace found 1,4-DCB levels ranged from five to 725 ppm. Occupational exposure of these workers lasted between eight months and 25 years. However, no time-weighted average daily exposure was determined. Blood tests and urinalysis did not show any indication of liver or kidney damage. And additionally, examination of the eyes did not reveal any damage.

In another study in a Taiwanese factory, the mean exposure was 11.8 years. Air monitoring for 1,4-DCB was not collected, although urine levels were analyzed for 2,5-DCP. White blood cell count and alanine aminotransferase were positively correlated with 2,5-DCP levels, suggesting possible liver effects. However, the authors did not report any obvious signs of illness in the workers.

[SLIDE CHANGE]

DR. RIMA WOODS: So NHANES population surveys have provided data for many published reports examining levels of chemical metabolites in urine that are associated with diseases or health conditions. And there are association studies which use urinary 2,5-DCP as a marker of exposure to 1,4-DCB. However, in general, a limitation of these cross-sectional studies is that the causal relationship between 1,4-DCB exposure and associations with health conditions in these population surveys are inherently difficult to establish due to factors such as exposure being based on a single urine sample, possible exposure to multiple pollutants, and misclassification of self-reported data.

Given these limitations, the increased 2,5-DCP in urine of adults has been associated with decreased lung function, increased prevalence of obesity, diabetes, metabolic syndrome, and cancer, increased risk for cardiovascular disease, and decreased kidney function, along with increased vitamin D deficiency.

[SLIDE CHANGE]

DR. RIMA WOODS: In children, increased 2,5-DCP has been associated with increased prevalence of obesity and hypothyroidism, and earlier age of menarche in adolescent girls. In pregnant women, increased 2,5-DCP has been associated with decreased birth weight in their

male infants, but not female infants, and increased prevalence for asthma, and rashes, eczema or hives in boys, but not girls.

While these cross-sectional studies contribute to establishing associations, the lack of exposure information and dose response precludes them from being used to derive RELs.

[SLIDE CHANGE]

DR. RIMA WOODS: So now, I'll move on to chronic exposure data from animal studies.

One of the few long-term, comprehensive 1,4-DCB animal studies was conducted by Aiso et al. and published in 2005. Exposures occurred in males and females of both rats and mice. Concentrations were 0, 20, 75 and 300 ppm for six hours a day, five days a week, for two years.

Necropsy conducted in all organs found treatment-related non-cancer lesions in liver of male rats and mice, the kidney of male rats, and the nasal epithelium female rats and mice, and the testis of male mice. Most of these effects were found only at the highest concentration of 300 ppm, although increased incidence of nasal and testis lesions were observed in the mid-dose groups as well.

[SLIDE CHANGE]

DR. RIMA WOODS: This table presents the main

chronic toxicity findings in male rats.

There was a positive trend for papillary mineralization and hyperplasia of the pelvic urothelium in the kidneys that was statistically increased at the highest exposure of 300 ppm. Hepatocellular hypertrophy of the liver was significantly increased at 300 ppm, but microscopic analysis did not find hepatocellular injury. Thus, OEHHA did not consider this a toxic effect of 1,4-DCB and did not consider it further for REL development.

[SLIDE CHANGE]

DR. RIMA WOODS: This table presents the main chronic toxicity findings in female rats.

There was a positive trend for olfactory eosinophilic globules that was statistically significant compared to control at both the 75 and 300 ppm concentrations. Specifically, the increased incidence for this nasal effect was for moderate and marked nasal degeneration combined. This type of lesion is age-related, but increased in incidence and severity with 1,4-DCB exposure.

Also in females, there was a positive trend for respiratory eosinophilic globules that was significantly increased in the 300 ppm group, as well as the incidence of respiratory metaplasia, which was also significantly

increased in the 300 ppm group.

[SLIDE CHANGE]

DR. RIMA WOODS: This table presents the main chronic toxicity findings -- let's see here. Whoops -- in mice. Gosh. Sorry. Lost this here. So sorry about that.

So this represents the noncancer findings in the two-year inhalation study looking at just mice. So in male mice we see hepatocellular hypotrophy at the high dose of 300 ppm. We also see testis mineralization at the mid and high dose for the male mice. And then in female mice, we do see metaplasia, of the olfactory epithelium, again just at the 300 ppm dose.

[SLIDE CHANGE]

DR. RIMA WOODS: So moving on to developmental and reproductive inhalation studies for 1,4-DCB.

A developmental inhalation study published by Hayes et al. in 1985 exposed New Zealand white rabbits to 0, 100, 300 or 800 ppm for six hours per day on gestational days six to 18. The only developmental effect found was an increased incidence of retroesophageal right subclavian artery in the highest exposure group of 800 ppm. This is a developmental anomaly of the circulatory system in which the right subclavian artery forms on the wrong side of the esophagus. In most cases, this anomaly

is without clinical symptoms, but in some cases may cause swallowing or breathing difficulties. The static -- excuse me. The statistical significant increased incidence in the 800 ppm group, not only for total number of fetuses, but also for total litters, led OEHHA to conclude that this was likely a treatment-related effect.

[SLIDE CHANGE]

DR. RIMA WOODS: There's also a two-generation reproductive and developmental inhalation study for 1,4-DCB in rats by Tyl and Neeper-Bradley from 1989. This is a study in which daily six-hour exposures of the F0 generation began 10 weeks prior to mating and continued through weaning on the F1 generation. The F1 rats in turn were exposed six hours per day until birth of the F2 generation. No reproductive parameters were affected by exposure, and there were recurrent acute affects in the high-dose group, which I mentioned previously.

The main treatment-related effects in the offspring included significantly decreased litter size in both F1 and F2 generations exposed to 538 ppm. Decreased body weight and weight gain was also reduced in both generations at the highest exposure to 538 ppm. And finally, there was an increase in stillborn pups and pup deaths during post-natal days one through four in both generations at the highest exposure.

[SLIDE CHANGE]

DR. RIMA WOODS: So now moving on to derivation of the REL values starting with the acute REL.

Developmental effects observed with exposure to 1,4-DCB can be used for acute REL derivation under the assumption that even just one hour of exposure during a critical window of development could result in developmental effects. The developmental effects observed in rabbits and rats were considered to be the most sensitive indicators of acute effects due to 1,4-DCB exposure, thus the increased incidence of retroesophageal right subclavian artery in fetal rabbits, and the decreased rat pup viability and body weight in the two-generation study were considered for the acute REL.

[SLIDE CHANGE]

DR. RIMA WOODS: U.S. EPA benchmark dose methodology was used to determine the point of departure, or POD, as opposed to using a NOAEL/LOAEL approach. A benchmark response rate, or BMR, of five percent extra risk was used to derive a benchmark concentration, or BMC, for dichotomous data, such as pup viability, where a pup died or didn't. For continuous data, such as pup body weights, a BMR of one standard deviation of the control mean was used to estimate the BMC. The benchmark concentration model then calculates the BMCL, which is the

95 percent lower confidence limit of the BMC. And this BMCL value is considered the point of departure for acute REL derivation.

[SLIDE CHANGE]

DR. RIMA WOODS: So as I outlined a few slides ago, both the developmental effects observed in rabbits and in rats were considered for acute REL derivation. In rabbits, the retroesophageal right subclavian artery endpoint was modeled using a benchmark response of five percent for dichotomous BMC modeling. Although there was a significant increase in the endpoint compared to control, the incidence was too low for adequate BMC modeling. Thus, a LOAEL/NOAEL approach was applied, giving a NOAEL of 300 ppm.

The pup viability was amenable to BMC modeling. Presented here in this table is the benchmark concentration modeling results for decreased pup body weight and decreased pup viability. The lowest BMCL is for decreased pup viability, which includes increased stillborn pups and dead pups during postnatal day zero through four in the F2 generation. The BMCL is 288 ppm, which is lower than the 300 ppm NOAEL from the rabbit endpoint, thus it will be the POD for the acute REL derivation.

[SLIDE CHANGE]

DR. RIMA WOODS: So to recap from the previous slide, the benchmark concentration, or BMC, is 464 ppm and the BMCL is 288 ppm. No time adjustment is made in extrapolating from six-hour exposure to a one-hour exposure for developmental studies, under the assumption that a single hour of exposure during a critical time in development could lead to the developmental effect.

Because the developmental effects are systemic effects, a default regional gas dose ratio, or RGDR, of one is applied. This default value is used when information for the human and animal blood-to-air partition coefficients are unknown, as is the case for 1,4-DCB.

[SLIDE CHANGE]

DR. RIMA WOODS: For the acute REL, the cumulative uncertainty factor is 200. This consists of an interspecies toxicokinetic uncertainty factor of two, which accounts for differences not addressed by the RGDR. An interspecies toxicodynamic uncertainty factor of root 10 was applied, which is the default value used for lack of interspecies toxicodynamic data.

An intraspecies toxicokinetic uncertainty factor of 10 and an intraspecies toxicodynamic uncertainty factor of root 10 were applied. These are the defaults used to account for differences between humans and accounts for

potential increased susceptibility of infants and children. This value is appropriate since the critical study used to derive the acute REL is based on a sensitive endpoint that occurs during development.

The adjusted POD of 288 ppm divided by the total uncertainty factor of 200 gives an acute REL value of 1.5 ppm, or 8,700 micrograms per cubic meter. This acute REL value is protective for sensory irritation and possible neurotoxicity observed at high exposures in rats, and is 10 times lower than the presumed NOAEL seen in some studies for irritation in human workers.

[SLIDE CHANGE]

DR. RIMA WOODS: For the derivation of the chronic REL, the two-year rodent study by Aiso et al. was chosen as the key study. The primary organs where toxicological effects were observed include the upper respiratory system, the kidney, and the male reproductive system. As was done for the acute REL derivation, a U.S. EPA benchmark dose methodology was used to determine the BMC and the BMCL for each treatment-related effect, with the BMCL used as the POD for REL determination.

[SLIDE CHANGE]

DR. RIMA WOODS: This table presents the calculated BMCs and BMCLs for the treatment-related effects seen in the Aiso 2005 study.

The BMC is the five percent response rate, and the BMCL is the 95 percent lower confidence limit on the BMC. The two lowest BMCLs, shown in bold in the table, are for mineralization of the testis in male mice and nasal olfactory epithelium degeneration, described earlier as eosinophilic globules, in female rats.

While the mineralization in the testis had a lower BMCL, the nasal effects in female rats was used as the basis of the chronic REL, because the final calculated concentration provided the most health protective REL value. This is due to the calculations used for determining human equivalency concentration, or HEC. The RGDR for the testis mineralization is one, as it's a systemic effect, whereas, the RGDR for the nasal olfactory epithelium degeneration is 0.2, resulting in a lower REL value. And I'll show these calculations in a slide or two.

[SLIDE CHANGE]

DR. RIMA WOODS: This is the graphed data for nasal olfactory epithelial degeneration, using the U.S. EPA Benchmark Dose software. 1,4-DCB concentration is on the x axis, and percent incidence is on the y axis. The open circles are the data points showing the incidence for the toxic effect at each exposure concentration of 0, 20, 75, and 300 ppm. The Benchmark Dose Program fit the blue

curved line to the data points, and calculated the five percent response rate, or BMC, which is the dashed green line in the lower left-hand corner. And the BMCL is the dashed orange line just to the left of the green dashed line.

[SLIDE CHANGE]

DR. RIMA WOODS: So if you recall from the earlier slide showing the modeling results, the BMC for this endpoint is 6.89 ppm and the BMCL is 4.65 ppm. A time adjustment of six hours out of 24 hours, and five days out of seven days is used to get an average daily concentration, which is 0.83 ppm. The human equivalent concentration is then applied using U.S. EPA methodology for the nasal airway. This methodology accounts for interspecies pharmacokinetic differences in respiration rate, or minute volume, and surface area in nasal airways of rats and humans. The resulting HEC, or human equivalent concentration, is 0.2, which is multiplied by the time-adjusted POD to give a value of 0.166 ppm.

[SLIDE CHANGE]

DR. RIMA WOODS: For the chronic REL, the cumulative uncertainty factor was 200, the same as that used for the acute REL derivation. The adjusted POD is 0.166 ppm is then divided by the cumulative uncertainty factor of 200 to give the chronic REL of 0. -- 0.8 ppb or

five micrograms per cubic meter. This supersedes the current chronic REL of 800 micrograms per cubic meter. For comparison, using the testis mineralization data would have given a chronic REL of 2.0 ppb, which is comparable to that derived from the nasal olfactory epithelium degeneration. And as such, both respiratory system and male reproductive systems are listed as hazard index targets for the chronic REL.

[SLIDE CHANGE]

DR. RIMA WOODS: For the eight-hour REL derivation, the same endpoint was used as that of the chronic REL - the nasal olfactory epithelium degeneration in female rats. For the eight-hour REL derivation, a time adjustment is applied, which assumes that a worker will breathe half of their daily air intake during an active eight-hour workday. And this adjustment results in an eight-hour REL of 1.7 ppm or 10 micrograms per cubic meter.

[SLIDE CHANGE]

DR. RIMA WOODS: So as Dr. Anastasio mentioned at the beginning, the public comment draft was released on November 29th, 2024 and initiated a 45-day public comment period, which ended on January 13th, 2025. And during that time, two public workshops were held. One written comment was received from CleanEarth4Kids.org. The public

comment letter received is available on OEHHA's website and contained four main comments. And I'll go through each of those four main comments and discuss OEHHA's response to the comments.

[SLIDE CHANGE]

DR. RIMA WOODS: The first main comment stated, "Children are particularly vulnerable to airborne toxins like 1,4-DCB. Their respiratory systems are still developing and they have higher respiratory rates relative to their body weight, which creates a higher health risk," end quote.

OEHHA is required by statute to derive new and updated acute, eight-hour and chronic RELs for air toxics, such as 1,4-DCB, using the methodology described in our noncancer technical support document adopted in December 2008. And this methodology explicitly considers possible differential effects on the health of infants, children, and other sensitive subpopulations, in accordance with the mandate of Children's Environmental Health Protection Act, SB25.

OEHHA's methodology also considers other sensitive subpopulations in addition to infants and children. In particular, Section 3.1 of the technical support document details how age-related sensitivities are taken into consideration to ensure that the noncancer

health values are appropriately and sufficiently protective of children's health.

The proposed acute REL is based on a developmental endpoint, for which increased susceptibility is already considered.

The proposed chronic and eight-hour RELs are based on degenerative changes in nasal epithelium of rats from a chronic study, where animals were treated starting at six weeks of age for up to two years. And while there are differences between the nasal epithelia of children and adults, such as children having lower densities of ciliated cells and higher levels of MUC5AC, which is a highly glycosylated polymeric mucin glycoprotein in the airway protection system, there is no evidence that children's nasal olfactory epithelium is more susceptible than adults. In addition, age-specific breathing rates and body weights are applied during exposure assessment.

[SLIDE CHANGE]

DR. RIMA WOODS: The second main comment stated, "The current REL proposals - five micrograms per cubic meter for chronic exposure and ten micrograms per cubic meter for repeated eight-hour exposure - do not sufficiently address the risk posed by higher exposure scenarios and should be further reduced to account for the significant indoor and occupational exposure documented

globally," end quote.

OEHHA develops health guidance values, such as RELs, for use in the Hot Spots program when assessing risk from stationary facilities in California. RELs are not developed for use in assessing risk from other emission sources or from contaminants in indoor air. Additionally, while studies of occupational exposure may be used in developing hot spots health guidance values, the values are not developed for use in occupational settings, which fall under the purview of CalOSHA. However, the eight-hour REL values are meant to protect people who may be exposed to emissions from a facility while at their workplace.

[SLIDE CHANGE]

DR. RIMA WOODS: The third comment stated, "There should be more comprehensive educational campaigns about the risks of 1,4-DCB exposure, and information about safer, non-toxic alternatives," end quote.

And while OEHHA acknowledges the importance of risk communication to the public, the draft document details the scientific basis and derivation of the RELs for 1,4-DCB, and educational campaigns are beyond the scope of the draft document.

And the fourth comment stated, "Additionally, there should be stronger air quality monitoring programs

in vulnerable communities to identify and mitigate sources of 1,4-DCB."

And air monitoring programs and mitigation are within the purview of CARB and local air districts. And risk management approaches again are beyond the scope of this draft document.

[SLIDE CHANGE]

DR. RIMA WOODS: And that concludes OEHHA's presentation on the draft RELs for 1,4-DCB.

And before I pass it back to the Chair, I'd just like to acknowledge Dr. Daryn Dodge, who is joining us online via Zoom. Dr. Dodge, who was the primary author for this document, has been a part of OEHHA's air toxics team for over 20 years. His contributions to the Hot Spots Program are immense, and he's participated in producing numerous technical support and guidance documents, some of which he has presented to the SRP. Daryn had the good fortune to retire from OEHHA at the end of December, and we're grateful that he's able to join us today. And so with that, we're happy to answer any questions and have discussion with the panel.

Thank you.

CHAIR ANASTASIO: Thank you very much, Dr. Woods. Just a reminder to the Panel, we're supposed to lever our video cameras on during the meeting. It's a State

requirement apparently. The second thing, I don't remember that the Panel gave Daryn permission to retire, so we might need to revisit that.

(Laughter).

CHAIR ANASTASIO: With that being said, I want to -- oh, good morning, Karen. Nice to see you. I want to turn it over to the leads this document, which were Mike and Pam.

Pam, would you like to it start?

PANEL MEMBER LEIN: Sure. Good morning, everybody. So, first of all, Rima, thank you for a really wonderful presentation. It was clear and easy to follow. I appreciate that.

So in my opinion, after reviewing the documentation that was provided to me, I believe that the -- OEHHA has used the appropriate methodology to reach these RELs. I find the RELs to be well-documented to be scientifically sound. And I have no concern with the RELs themselves or how they were derived. I would point out, however, that I think the rationale for excluding specific endpoints or specific studies was not as well articulated in the document as they were in today's presentation.

And so, I would potentially urge the OEHHA staff to go back and review the document, particularly on page 10 in the -- well, I guess -- I don't -- what do you call,

the preface, where you sort of provide a nice summary of the RELs and how you reach them. There's really not any sort of rationale provided why you excluded the human studies, why you focused on rat, and why you chose some of the endpoints that you chose for your -- for your analysis. So I think that was the only substantive suggestion that I have to improve the documentation.

And that's pretty much all I have, Cort.

CHAIR ANASTASIO: Okay. Great. Thank you, Pam. And, OEHHA, that comment makes sense?

DR. RIMA WOODS: Yes.

CHAIR ANASTASIO: Okay.

DR. RIMA WOODS: We can revise the entry portion of the document so that we can include more information on why certain studies were excluded. And throughout the document as well, we'll confirm that we have the rationale stated clearly.

PANEL MEMBER LEIN: Yeah. It was -- it was good in some places, but missing -- it was inconsistent I guess is the best I would -- I would phrase that. So to make that more consistent would definitely strengthen and bolster your analysis, I think.

DR. RIMA WOODS: Thank you.

CHAIR ANASTASIO: Great. Thank you, Pam. Just a note here for legal purposes, just to say that Dr.

Landolph can't turn on his camera, in part because of impacts from LA fires. So he has tried, but it's not working, so that's as good as we can get there.

Okay. Mike, comments.

PANEL MEMBER KLEINMAN: Yes. Thank you. I agree completely with all of the comments that Pam made. And so I'll just -- well, I also have problems following the argument for the choices in setting up the acute REL. And so I -- you know, I think the way it was presented this morning made it much more clear and, you know, much more well justified. But as an exercise, I went back and looked at some of the other acute exposure data. And as it turned out, looking at a collective departure as a LOAEL of 50 ppm based on occupational exposures, and sensory irritation, and putting in an intraspecies toxicokinetic factor of 10, and an intraspecies toxicodynamic factor of root 10, came up with a cumulative uncertainty factor of 31.6, which would give us an acute REL of about 1.6 ppm.

So, you know, what I got out of that was the data are very consistent, you know, from the very -- going across. Now, maybe that's serendipity, but it made me feel better about the way the numbers worked out.

So I agree that strengthening up the discussion of the choice of the acute data used for the REL will make

it a lot clearer. And again, I wanted to congratulate everyone on a very clear and well done document. It was actually nice to read. And I picked up a lot of the terminology. So thank you very much. That's it.

CHAIR ANASTASIO: Great. Thank you, Mike.

I'm just going to go Round Robin now through the rest of the Panel and see if people have comments. Paul, would you like to start.

PANEL MEMBER BLANC: Happy to. So let me start by echoing and amplifying Dr. Kleinman's comments and specifically urging the document to be edited to present the alternative calculation based on the human eye irritation NOAEL of 50 parts per million even if OEHHA has concerns about the paper not providing sufficient details of the measurement itself methodology, because I think it's quite a -- strained to make the argument that even one hour of exposure could be causing the developmental abnormalities that were used from something which is not an acute exposure, but is over many days. And it's up to OEHHA if they actually would substitute the 50 parts per million LOAEL approach, but certainly presenting it in parallel as a justification I think would reinforce.

And just as a general principle, I don't find the benchmark dose methodology so compelling that one should jump through hoops to use a study with multiple levels of

exposure, if it really doesn't fit the need of what the acute exposure is. That's just my own comment. I think somehow that drove OEHHA in a way that may be counterproductive. If all you have is what can provide a NOAEL- or LOAEL-based approach, I think that's still okay, if the tradeoff is worse. So that's my comment in that regard, just reinforcing what Mike Kleinman said. So I don't it's just explaining. I think they should provide in parallel what the alternative calculation would be, and they've done that quite frequently in these documents. So I don't see it as precedent setting.

I want to also circle back, and maybe Dr. Lein would like to comment on this as a neurotoxicologist, I think OEHHA should be credited with calling out leukoencephalopathy as a toxic effect. But I think in doing so, they have overly muddied the waters by implying that it's not specific and many things cause it, neither of which is correct. It's a really specific clinical, and radiologic, and pathologic finding. And there aren't that many things that cause it. And most things that cause it are actually pharmaceuticals, chemotherapeutic agents, and an important drug of abuse called Levamisole.

So it's not a generic, nonspecific, common environmental toxic endpoint. It's rather startling actually in terms of this particular chemical. And it's

been reported repeatedly. I would actually urge, not only that that wording be changed, so that it's not downplaying the significance of this endpoint, but actually providing a small table of the cases that they cite would be helpful.

I would also note that they've really missed a more recent case, which was from 2018 in Neurology, a major journal. And it's a child with this endpoint, who was also, for psychological reasons, abusing the mothballs. And that's, author Patel, Neurology, 2018. It's called, *Clinical Reasoning: 12-year old girl with headaches and change in mental status*. Well, when you read the actual clinical case, they very well document that it's leukoencephalopathy.

Also, I'd point out that what you've seem to have done is gone only back as far as 2015 or 2014 and nothing before, which is okay, but you should say, we -- you know, we have not cited anything before this, although there are others, because there are some that are actually quite important case reports, including 2009, Kumar and also in -- I believe it was in Neurology, so -- in major journals.

So, kudos for shouting out leukoencephalopathy, but please I would say make it even stronger, that section. This is a very important endpoint. It may not

be that relevant to your endpoint numbers, but for other health protective regulatory reasons, I think it's really important. And I just -- I have other comments, but I'd stop there to give Pamela a chance maybe to comment for a neurotoxicologic point of view.

PANEL MEMBER LEIN: No, I think you're absolutely right, Paul. This is a relatively unique neurotoxic outcome. It is associated with a relatively small subset of environmental chemicals, mostly solvents. And I guess I didn't really bring it up as a question mark specially, because again the point of this exercise, which is to derive RELs. However, I do think it's harkening back to my comment that you provide a really strong rationale for the studies you chose to -- that to use for deriving the REL and why you excluded others, because this is a very unique endpoint and kind of jumps in your face.

And when I think about this particular compound, of course I'm biased because I'm a neurotoxicologist, that is the endpoint I think of. But again, it's typically higher exposure levels, so -- but I do think it would be worthwhile to call this out. And I agree with Paul, it is a relative unique endpoint of neurotoxicity.

PANEL MEMBER BLANC: So let me -- thanks. Let me go through my other points. This is a small one, but actually touches on the very same issue, because it has to

do with the mothball abuse syndrome, which they don't use that term, but it's been used in the literature. There -- you -- the term "incidental ingestion" was used -- you know, "accidental" and "incidental". I don't know what incidental means, because it's intentional. I wondered if that was a typo for "intentional". It's an abuse situation. That's why there's such high levels of exposure.

Unrelated to that, I want to ask a little bit or comment about the metabolism and the CYP section. So when it's first brought up, it just talks about CYP generically. And, you know, I wrote note to myself, well, which one? And then a couple of pages later, it starts talking about specific isoenzymes. So -- and makes the point that CYP2E1 is the dominant human isoenzyme for metabolism, but then says a little bit later, or indicates a little bit later, that another of the enzymes also is at play in human metabolism. I think that section could be a little bit clearer, because it's mutually -- what does dominant mean? Does that mean 51 percent or does that mean 98 percent?

And beyond that, it's not really clear to me from the document. Is it the assumption that it is the metabolites which are responsible for toxicity and the native unmetabolized compound is not toxic? You know, eye

irritation is likely to be just from the parent compound, I would -- I would guess. I don't know for sure. But it would be good to say explicitly, you know, what the issue is. Why? Because for some of these isoenzymes, a lot of people are on medications, humans, that would inhibit the enzyme or induce the enzyme. So that speaks to the spectrum of vulnerability in the population. And I might also say that the -- there was no explicit comment on the storage of the parent compound in fat that might have implications for vulnerable subpopulations. Does that mean that since half the population is overweight, or more three-quarters, that those people who would be more at risk from exposure to this chemical, because they would store it or what?

And similarly, the data from the national metabolite sampling that shows a 50 percent fall over the last 20 years, I'd be very curious -- I mean, there's no -- you don't have an explanation, but there isn't really any comment on even theoretically what might that be due to, given the uses of the chemical that you've described. Have market sales of this product as a deodorant and as a mothball fallen 300 percent over the last 20 years? Is there some -- what is the reason and what is the source of exposures that might account for that?

Also, I'm assuming that where mothballs end up is in a landfill. Is any of the hot spot data that you have relevant to landfill disposal of this chemical, is there -- are there higher levels or any levels detectible near solid waste landfill?

Your -- the comment in the -- in the oral presentation, which I didn't actually catch in the written text, it may be there too, that a problem with population-based levels is misreporting of exposure is completely irrelevant to biological monitoring. I mean, that's what it is. It doesn't matter if they reported it or they didn't report it. If the argument in favor of biological monitoring is that you're independent of self-reported exposure, it is what it is. So if that's in the text somewhere, it doesn't -- it really shouldn't be there.

I think that's mostly my comments. One other area that I should mention was it was stated fairly explicitly that dermal absorption does not occur with this chemical. And that may be true, but -- because I certainly couldn't find anything in the literature on it, but what is that based on? Is there a study that actually -- an experimental study that showed it doesn't pass the dermis? I'm just curious if that's -- if we're sure about that. It's also a comment not relevant to your

REL derivations, but just from a more public health protective thing.

And then the other question that came up, as I saw the presentation that I didn't really clue in on as I read it, is these tests for trend that you show with the tables, I understand the pairwise comparison between highest and lowest. And when you have three levels of exposure and there's zero cases, zero cases, and then 20 percent incidence, and you say the trend is positive, it actually surprises me a little bit that the statistics of that are positive. It doesn't really suggest a trend. It's just one out of three is elevated. So, I'm wondering what -- was that a nonparametric test of some sort or an inappropriate use of a parametric test? How was that -- how was that done? Was it a chi-squared test for trend or something? It just -- it surprised me a little bit on those, and that's just technical question. Maybe the biostatistical person on the Panel can comment on that.

That's it.

CHAIR ANASTASIO: Thank you Paul. Karen, you want to talk about the last point and then I'll ask OEHHA if they want to have any responses.

PANEL MEMBER MESSER: Yeah. I'm happy to look into it. I think the test for trend wasn't specified. Oh, here it is, the Cochran-Armitage Trend Test. And, you

know, that test can be positive when there's not a linear trend, when you've got some bouncing around and then something increases on an extreme category. So that's not unusual to have that occur.

It's a matter of interpretation how you might interpret that. So I'm happy if there are some specific instances where you think the interpretation might not be reasonable. I'm happy to look at that. So, you know, if you just send me some page numbers, I'll take a look.

CHAIR ANASTASIO: Thank you, Karen.

Rima or anyone else from OEHAA, any responses to Paul's comments?

DR. RIMA WOODS: Thank you, Dr. Blanc for all of the comments. So I think that we will definitely look into adding one of your first points was providing the alternative calculations based on the human studies. So that's something that we can add to the acute REL derivation section to sort of give it some context, when an equivalent acute REL could be based on those occupational studies.

And then for the leukoencephalopathy point, we will definitely go back and revise that section and maybe we'll look for the studies that you mentioned and then any additional case studies that we can find, and then maybe strengthen the link within the document for

leukoencephalopathy to 1,4-DCB. Is it -- you mentioned it sounded like we downplayed it a bit. So we'll make those revisions to strengthen that connection.

And then for the metabolic issues with the cytochrome -- with the CYP2E1, we can go back and again revise that section as well, make it clear, bring the main isozyme up front and maybe do a little more explanation and be a little more clear with primary, predominant CYP versus any additional CYPs that might be involved. So we can -- we can sort of strengthen that as well.

And as far as the NHANES date with the reduction, we could do some digging to see if we can find any supporting information for what may have caused the decrease in the biomonitoring levels. And then, let's see, I know that there is a downward trend in use, so 50 percent decrease, just based on some information we found pretty quickly. It looks like there's been a 50 percent decrease in the total amount.

Is this the geometric mean? Yeah. Okay.

So -- oh, yeah. So, we're looking at between two to five times decreased use in terms of millions of pounds in the U.S.A. And so there just seems to be a huge decline in the use. I know California banned the use as air -- indoor air fresheners back 2006. But we can maybe bring in some information for nationwide -- a sort of

nationwide view.

PANEL MEMBER BLANC: That would be -- that would be great, because I think that strengthens the importance of the whole topic, in a way.

DR. RIMA WOODS: Great. Then we'll do that.

And then just the last point I know you had mentioned dermal -- the dermal exposure issue, our point about dermal absorption being low, it was based on a study in rats with looking at the lethal dose for rats. And it was very high by the dermal route. It was more than six grams per kilogram. And so based on that, we determined that the dermal absorption for unbroken skin, of course, is very high, so -- but we can add additional information related to that, if you think, that would be helpful.

PANEL MEMBER BLANC: I think it would be, and also because one of the toxic effects you showed was -- in humans was dermal --

DR. RIMA WOODS: Dermatitis.

PANEL MEMBER BLANC: -- dermatitis, so, you know, the chemical causes a condition which would promote its determine absorption, if that's true, right?

DR. RIMA WOODS: Yeah. No, that's great point. Yeah, we can been definitely strengthen that. I know the dermal route we don't spend too much time on. It's not a relevant, but yeah, in this case, in light of the

dermatitis, we could definitely add that. So thank you.

And that's all I have, Cort, unless anyone else has anything to add?

CHAIR ANASTASIO: Okay. Great.

Thank you very much, Paul.

Kathy, comments.

PANEL MEMBER HAMMOND: There we go. Trying to unmute there. Sorry.

No. I think this is very interesting and important work. What I was missing was there's nice information about the concentrations in the air, indoor and outdoor, and also the studies that have related the air concentrations to urinary concentrations, which is important, given that the most widespread information we have is urinary from NHANES. And it seems like -- it seems to me like it's important to circle back, having come up with a REL, and think about what -- how does this REL relate to what we know about exposures. As so in my kind of rough looking at that, we are -- we are looking at the general population.

Now, actually, I was wondering with the hot spots, are we only concerned about outdoor air, is that correct? And this is basically -- it's pretty clear it's an indoor air source, both from the measurements that have been made and what we know about the sources. So

occupation -- people are exposed occupationally, and people are using exposed in their home due to products that they're using. So the actual -- you know, is it, is it appropriate? Is it appropriate to discuss the fact that the indoor air concentrations, which are not hot spots, are actually getting close to the RELs, you know, in some cases exceeding them?

So, you know, the mean indoor in the 1987 Wallace study was six -- well, let me back up. It's pretty clear looking at the urinary and all of that -- well, that there is a correlation between urinary and airborne. The levels that are indoors -- that were measured indoors in '87, were 6.2 ppb, and the chronic level being suggested as 0.8 ppb and eight-hours is 1.7.

And then the -- I know the levels are falling indoors. And then the classroom levels were actually a mean of 0.43, which is half of the chronic but if we look at the eight-hour, it was a max in one school that was just about at the eight-hour suggested REL. So children in schools, you know, that is of concern. Again, that's an older study and again that's indoors.

So I'm not sure, but it just feels to me like that this information could be brought together at some point in a concluding paragraph to say that these are the RELs, that outdoors doesn't look like it's a major source,

but with all the work that you've done that's so important, it's worth identifying the fact that indoors really get above the RELs. I don't know if that's actually -- but maybe that's not appropriate, but just from a public health point of view, it feels important to me.

CHAIR ANASTASIO: Thank you, Kathy.

Rima, any response? Any --

DR. RIMA WOODS: Yeah. No, I mean, I think it's a really important point and it was brought up also in the public comment that we received. And so we do develop the values under the Hot Spots Program, you know, but the RELs should be health protective regardless of the exposure source. So they are meant to be applied, you know, derived to be applied to facilities emitting, but we consider them health protective regardless of where the exposure is coming from. So I think that's an important point to make.

And, I mean, we can discuss, you know, maybe adding something into the document where we acknowledge that indoor air is -- could be a major source. You know, but again, since the focus is to derive it for the Hot Spots Program, we're kind of in a, you know, sort of a gray area, I agree, so...

PANEL MEMBER HAMMOND: And are there -- yeah. I

wasn't sure -- have measurements been made specifically to be near the known sources? So I missed it if it was there.

DR. RIMA WOODS: No. So there is one current situation of air monitoring. So 1,4-DCB is part of the list of VOCs that are monitored for in the SNAPS program, which is under AB 617. And so that's the Study of Neighborhood Air near Petroleum Sources. And so these are communities that are located near petroleum sources, oil wells, refineries. And 1,4-DCB is monitored. And I believe there was one location where they did detect it. I don't know how many locations they monitored for that, though. And so --

PANEL MEMBER HAMMOND: I think that's the -- that is at the heart of the Hot Spots is deciding what are the -- we've talked about, in a different way in other meetings, the importance of including communities' concerns. And I think what we need to do in a hot spot is to identify as much -- as well as we can, where are the places that the community could be exposed to higher levels, what are the hot spots for this compound? And I don't think that that was laid out very clearly what you just said.

DR. RIMA WOODS: Yeah, we can definitely make mention of the SNAPS monitoring into the document as well.

PANEL MEMBER HAMMOND: Yeah. Thank you.

CHAIR ANASTASIO: Thank you, Kathy.

Beate.

PANEL MEMBER RITZ: Yeah. So thank you for a well-written document. I enjoyed reading it. Whenever I see pesticide, I wonder what it is that causes the pesticide action, right? And this is a moth repellant, but it's also actually killing them. So I went back to the literature to figure that out, because it's not in the documents. And it seems that the mode of action is through oxidative stress handling or inducing, as well as calcium handling and adenosine receptor inhibition that contribute to calcium handling, which all, of course, are modes of action that affect the nervous system, which then would logically again support the neurotoxicity of argument for this.

The other -- and I think that would be actually nice to mention, so we don't just have people who are addicted or psychologically disturbed and eat mothballs who have leukoencephalopathy, which is a really serious outcome, but then may be more minor neurotoxicities that together with other substances could also eventually cause neurotoxic action at different, you know, developmental stages or during neurodegenerative action.

And that actually brings me to the other one.

When I saw CYP2E1, I thought, oh, that's one I know, because it's important for Parkinson's. It's very much expressed in the areas of the substantia nigra, and it's an inducible enzyme, and it does cause oxidative stress and mitochondrial inhibition. So again, you know, if this is an agent that induces this CYP, then I would say we should be worried about it more, as well as the nasal route, because we are now thinking that, for example, neurodegeneration like Parkinson's is being induced through the olfactory bulb, which also cam out in some your animal studies.

I'm not saying this is happening. I'm just saying it made a lot more sense for me to put these pieces together and maybe there's some space to actually do that in this document to link these neurotoxic actions a little bit better.

And otherwise, yes, I was very concerned when I then also read that NHANES finds it in just about every urine sample, and very glad to see that it has been going down, but it's still around, and, you know, so that is something we should -- we should make that circle again that Kathy has suggested. That's it.

CHAIR ANASTASIO: Thank you, Beate.

DR. RIMA WOODS: Thanks for those comments. We can look into adding the pesticidal mechanism of action

into the document and some of the background just so that it's clear that there is, you know, neurotoxic mechanism in the insects, just so that we clearly lay that out.

CHAIR ANASTASIO: Pam.

PANEL MEMBER LEIN: I just would add to that, however, that oxidative stress is not a uniquely neurotoxic effect, and that this could actually explain some of the other systemic effects that you're seeing in both the human and the rodent studies. And it's not clear actually that the insecticide is really a neurotoxic effect. There is some indication that it could also be due to effects on the GI system, for example, in these insects. So I would -- I would caution you against making a strong link to the neurotoxicity, which does not appear to be one of your more sensitive endpoints, but it would be interesting, I think, to include information on what is known about the mode of toxicity or mode of action just to say that there is -- there's a biologically plausible explanation for how this compound could be causing these effects.

CHAIR ANASTASIO: Thank you, Pam.

Okay. Ahmad, your turn.

PANEL MEMBER BESARATINIA: Oh, good morning. Thank you again. I echo the comments of other Panel members regarding the extensive work that went into

preparation of this document. Very nice read. I have a general comment and a couple of comments regarding the content of this document.

First, the general one. I have noticed that there has been a steady decrease in the number of comments and feedback that you receive from the industry and stakeholders on these technical support documents the past few years. I remember we used to receive several, you know, responses and comments from the industry on these types of document, some of which were very relevant, some of which were very informative providing a different perspective and making it possible to have a -- you know, a different -- look at the different point view and have a fruitful debate.

I'm wondering has there been any change in the way that these documents are communicated to stakeholders and the industry, and the opportunity for them to comment on this and respond to this, and is there any specific reason why we are not receiving comments from them?

DR. RIMA WOODS: Yeah. So I can just say this. We haven't changed our -- you know, our approach to releasing the documents. When we release them, we put them on our website. We announce through a listserv. We also publish a CRNR notice so that goes into the registry for California. So we are still following the same, you

know, approach that we have used for previous documents. So I don't have an answer for why we have received less.

We are still holding two public workshops. So we hold one in Northern California, one in Southern California, and actually we've tried to increase outreach by making sure that our Northern California meeting is hybrid, so folks can tune in online. They can email questions in live. We can answer them live during the meeting. Whereas, prior to COVID, they were in-person only and then during COVID, they were just by Zoom. So we've done our best to make sure that those who would prefer to attend virtually still can do so for at least one of the two workshops.

PANEL MEMBER BESARATINIA: Thank you for clarifying it. Just a couple of questions with regard to the document itself. The first one is with regard to the presentation of data in Table 1, which is in page 13. My question was whether the data that are presented here -- because I see some missing data. For example, if you look at this table, it goes from -- in row four, it jumps from 2004 to 2011. There is a like six-, seven-year period missing data. I'm wondering whether this is because you selectively presented this data or this data were not available to you, and that is why they're not included?

And my second question with regard to this is,

also I see that in the second column when you're providing data, specific for age, you are presenting it as old versus children. Since you are putting so much emphasis on vulnerable populations and the susceptibility of the children as compared to adults, I'm wondering wouldn't it be more appropriate to show the data for adults versus children, because old would include both adults and children? So we would get a better idea how these levels through the years changed in adults versus children of those ages, because I see the data for children from 2003 up to 2016, are stratified for age six through 11, and 12 to 19.

And I had one more question. Maybe you can respond to this and then I will follow.

DR. RIMA WOODS: Yeah. So we did our best to try to represent as much data as we could from NHANES in a single table, which was rather challenging. So we can go back and confirm that we're not excluding any data. As far as I know, this is the data that was available to us. And we did try to break it up for the intermediary years for just children ages six to 19, as you mentioned how we have those sort of broken out. And so we can look back and confirm the data for adults alone and represent that as well, so that you can see a comparison, rather than lumping them into all.

PANEL MEMBER BESARATINIA: Thank you. That would be helpful if the data are available. I think their inclusion in this table would be very helpful.

My last question is on page 19 of this document. You have stated that there are limitations in one of the study, Hollingsworth. And the second part of that paragraph indicates that, "Concentration data is listed as concentration ranges with median values, in which peak exposure concentration cannot be determined, and therefore a clear qualitative correlation between concentration and the sensory irritant effect cannot be corroborated." So my question to you is why is it necessary to have the peak concentration in order to evaluate the correlation between these two variables, because clearly, you have the median value and you have the range. One would -- could argue that you don't really need the peak. You can easily use even the lower range in order to be, you know, extra conservative in evaluating. Can you clarify this for me?

DR. RIMA WOODS: Okay. So that's a good point. I think we can revisit that study and take a look and see if possibly using the average concentration or, as you mentioned, the lower range -- or the low end of the range could provide us with a different way of looking at the data. This is one of the older studies with some limited information. And so, yeah, I think it would be good if we

could go back and take a look at that study and see if there's another way that we can look at the data, rather than just saying the peak data is not there, so we can't use it.

PANEL MEMBER BLANC: I just want to chime in. Paul Blanc here. Isn't that the study we've been talking about in terms of the parallel calculation or have I lost track?

DR. RIMA WOODS: No. I believe that is the study with the 50 ppm was determined.

PANEL MEMBER BLANC: Right. I mean, we're all -- it is all the same study or are there two different occupational studies with eye irritation?

DR. RIMA WOODS: I'd have to double check on that.

PANEL MEMBER BLANC: Yeah. I mean, it just -- it just underscores the importance of what Ahmad is saying, because, you know, you don't want to cut the ground out from underneath that study in such a manner that you can't use it at least for parallel calculation, if that is indeed the same study, because that was my memory of it, but I don't have the whole thing open in front of me. And I think part of the problem is the use of the word "correlation" in a nonscientific way as opposed to the implication of a scientific correlation. I think that's

the point. The -- correlation literally is not what you meant there. You meant -- I don't know --

PANEL MEMBER MESSER: Association.

PANEL MEMBER BLANC: -- association or something. So that I think got you into trouble a little bit.

CHAIR ANASTASIO:

PANEL MEMBER BESARATINIA: Thank you. That's all I had. Thank you, Cort.

CHAIR ANASTASIO: Great. Thanks very much, Ahmad.

Karen.

PANEL MEMBER MESSER: Yeah. I found the exposition to be very clear in this report. As my colleagues did, I had a little -- I didn't find statistical issues. I thought the statistics were clearly described. I do see what is troubling, Paul, with going back and rereading. I see what's troubling him with the presentation of the trend results and I can make just a suggestion about how to present those results so that they don't raise the confusion. I think what's happened there, there's a statistical trend across quartiles. And then to summarize the strength of the trend, the report presents odds ratios from the last to the first quartile. And I think that's a good summary statistic, but it doesn't necessarily describe the trend. So I -- I'll make a

suggestion about how to word that presentation. I think it's very good actually.

Along with Dr. Hammond, I had a little bit of trouble figuring out the public health importance of the issue, just getting a sense for it, because it seemed like the exposures were from eating mothballs or other acute extreme exposures, and there wasn't a lot of information about occupational exposure or just ambient exposures. So that was just a general comment. It was hard for me, especially in light of the tenfold reduction in urine levels in adults, it was a little hard for me to get a feeling for the public health importance of this particular compound. But I found the report to be very clearly presented and I didn't identify any statistical issues.

CHAIR ANASTASIO: That's great. Thank you, Karen. It is always fantastic to have a statistician weigh in on statistics. So thank you.

Joseph, it's nice to see you.

PANEL MEMBER LANDOLPH: Nice to be seen.

(Laughter).

PANEL MEMBER LANDOLPH: Thank you, Cort.

I thought it was a terrific document, as everybody else did. I thought a huge amount of work went into it, and I was very pleased to be a reviewer. The

scientists, of course, that wrote it, Daryn Dodge, and the technical reviewers, John Budroe, Martha Sandy, Dr. Woods, are all terrific scientists and they did a terrific job writing and reviewing this. It was a very clear document to me as well. The summary was clear. The major uses, and occurrence, and exposures were clear. Toxicokinetics was clear. Acute toxicity of 1,4-DCB was very clear and so was the chronic toxicity of this compound, the developmental and reproductive toxicity, and the derivation of the reference exposure level. So it was a pleasure to read and I didn't have too many problems with it.

I'll just mention one or two very small things, but they are very small. I guess it was on page -- let's see, page eight on lines 324 to 326, it says, "Microsomes produced the least reactive metabolites." It's a phrase. It should be microsomes producing the least reactive metabolites, and I just want to make the grammar as fantastic as the rest of the document.

The -- I think metabolic scheme was correct and drawn in detail from the literature and was very good. It help me to read through the document, so I was very happy with it. I don't think there was anything I didn't really, really like.

I would suggest, just as a friendly reviewer, in

the future, that I understand you said you wanted to present some things by themselves or congregate -- add it together with other things, and I had a little bit of trouble when you did that, because I was trying to follow the -- what you were talking about in the original tables and I got lost a couple of times. So to the extent that you can, I would recommend that you refer to the actual tables or you can say an aggregation of two tables, 1, 2 and 3, or something like that. Otherwise, it's a little tough to read it, you know, keep up with you when you were giving such a nice presentation.

So in general, I don't have any dramatic comments to make. They're all very small. I thought the document was good just like everybody else did, and I was pleased to read it. It was very informative, and that's about all I have to say.

Cort, do you want our written comments or is what they get from the transcript good enough?

CHAIR ANASTASIO: Rima, would prefer comments in writing?

DR. RIMA WOODS: If there are additional comments, or as Dr. Messer had kindly offered to give us a suggestion for wording, we're more than happy to take them written. We will also refer to the transcript when we receive it to make sure that we hit everyone's comments.

So if the Panel would like to send us written -- a written version of comments, we'd be grateful, but not necessary.

PANEL MEMBER LANDOLPH: Yeah. Okay. I'll do that then. I'll send you some written comments as well.

CHAIR ANASTASIO: Yeah. Great. Thank you very much, Joe. So I echo what the Panel has already said about this being a very clear, well-written document. I have just some minor comments that are not worth discussing, so I'll send them via email in written form.

So that wraps up our discussion. Any final comments from the Panel before we go to public comment?

Okay. Seeing none, Hnin Hnin, will you describe how one can give a public comment.

DR. HNIN HNIN AUNG: Thanks, Cort. Yes, I will. We'll now recommend for this item will be open. To participate, please raise your hand using the raise hand icon. I will call on you in the order that the hands are raised and we will unmute you when it is your turn to speak. Each speaker will have two minutes to share their thought comments. A reminder will be given 30 seconds before your time is up. After which, you will be muted. Thank you for participation.

CHAIR ANASTASIO: Well, we'll give people a minute or two to raise their hands.

DR. ARASH MOHEGH: Can people raise their hand in

Zoom? It's possible.

DR. HNIN HNIN AUNG: Yes.

Okay. So I saw one. Thank you. Please, I apologize if I don't pronounce correctly. So you can you unmute. I think we have to unmute. So by will unmute you and you can speak. We will -- I will remind you again that we will remind you 30 seconds before your time is end and then we will mute you.

DR. HNIN HNIN AUNG: Yes, you can.

Did you unmute already. Yes, you can. You can start to speak.

BYANKA SANTOYO: Good morning. Thank you so much for all this information. I've been listening to it. I'm also part of the AB 617. I'm a community organizer for Center Race, Poverty and the Environment.

My concern about this toxic is that if it's going to be placed on the pesticide notification as a restricted material? I know that in -- I was listening to the Panel how they were mentioning children being exposed. And it's concerning when we are in the Central Valley and pesticides are heavily used in the area. And as us parents, I'm calling myself in this mix, but as us parents do not know what our children are being inhaled or our families are being inhaled.

One question, is DPR going to be involved in this

process for the pesticide review panel, the review -- or, I'm sorry, the review or -- and if so, would it be placed on the pesticide notification system? I know that they're only doing a limited amount of pesticide notification for when it starts in March, but it would be interesting to see if there is any facilitation for parents or schools to know that there's this pesticide near their school settings.

CHAIR ANASTASIO: Thank you, Byanka, for your question. This is actually more of a Department of Pesticide Regulation question. And I'm not sure, OEHHA, do you feel comfortable addressing the question?

DR. RIMA WOODS: So the document is developed under the Hot Spots Program, and the Hot Spots Program doesn't have much interaction with DPR. So I think it would be best, yeah, to definitely reach out to DPR and request information regarding any use that they're aware of, and if they plan to put it on the notification system, but we wouldn't have that information unfortunately.

CHAIR ANASTASIO: Yeah. Just to mirror what Kathy and others have said, Byanka, is, you know, one of the major exposures is from indoor air. So use of products that contain 1,4-dichlorobenzene is one of the major routes where people get exposed to this. So if you can be careful about what you bring into your home, that

should really reduce the levels that your children are exposed to.

All right. Thank you Byanka. Hnin Hnin, do we have additional comments?

DR. HNIN HNIN AUNG: No. Please raise your hand if you want to comment.

CHAIR ANASTASIO: Hnin Hnin, do I take that as a no?

DR. HNIN HNIN AUNG: Yes. No. Yeah. We haven't -- yeah.

CHAIR ANASTASIO: Okay. All right. Then we will close the public comment time and we'll move on to our final piece, which is consideration of administrative matters.

First, just an update. If you remember, we met in August 2024 to consider the isoprene IUR. Just to give you an update on that. It's been revised, and finalized, and approved in November. So isoprene is finished.

Number two, the advisory bodies, such as the Scientific Review Panel have been given permission to continue to meet remotely through December of 31st of 2025. So I expect that we'll have at least one other meeting before then. And so the plan will be to have that over Zoom as well.

Next, just to reiterate, the terms for many of us

have expired and progress has been slow. I'm going to reach out to members whose appointments have expired and asked you if you have suggestions for new members who might take your position. And I'm hoping this will move the process forward a little bit. If you're interested in being reappointed - for example, I think Mike is. Thank you very much, Mike - then just reiterate that in the email, and that would be great, because that should make things go more quickly, and it would be great to have you continue.

Final piece, I know that at least some of our Panel members have been terribly effected by the fires in Southern California, and I imagine the same is true for other people on our call today, including possibly agency staff. And I just want to say on behalf of the Panel, really deeply sorry for your losses. And I hope the recovery is not too long and too painful, but we're definitely thinking about you.

Those are the only administrative matters that I had. Are there any items from the Panel administratively?

Okay. Oh, one thing I forgot to do, which I always forget to do, a decision on how we will proceed with today's item and the revisions. So our standard procedure for items that are for straightforward, such as today's, has been that OEHHA revises the document, they

send it out to the leads and me, and then those people give their thumbs up or have alternative or additional comments. And then we just do it -- the final approval over email. Is that acceptable to the Panel?

PANEL MEMBER BLANC: Yes.

PANEL MEMBER LANDOLPH: Yes.

PANEL MEMBER MESSER: Yes.

CHAIR ANASTASIO: Okay. Great. If definitely saves us time.

PANEL MEMBER RITZ: Yes.

CHAIR ANASTASIO: So, Rima, we'll proceed the way we've been doing.

That's all I have. So if there are no other items, can we get a motion to adjourn?

PANEL MEMBER BLANC: I so move.

PANEL MEMBER LANDOLPH: Second.

CHAIR ANASTASIO: Second. Excellent. All in favor raise your actual hand?

(Hands raised).

CHAIR ANASTASIO: Okay. We're unanimously in favor of stopping.

Fantastic. I want to thank all the Panel members. Appreciate that. I want to thank OEHHA and all the staff for your work on this document and I hope everyone has a great rest of your week.

Thank you, all.

(Thereupon the California Air Resources Board, Scientific Review Panel adjourned at 11:10 a.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 3rd day of March, 2025.

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