MEETING

STATE OF CALIFORNIA

ENVIRONMENTAL PROTECTION AGENCY

AIR RESOURCES BOARD

SCIENTIFIC REVIEW PANEL

ON TOXIC AIR CONTAMINANTS

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

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I N D E X

I N D E X C O N T I N U E D

P R O C E E D I N G S

CHAIRPERSON ANASTASIO: Okay. Good morning, everyone. I'd like to call the meeting of the Scientific Review Panel to order. Welcome to everyone on the webcast. Welcome to everyone here in person. Let's just go around the room and state your name and affiliation. I'm Cort Anastasio from UC Davis, and Chair of the Panel.

PANEL MEMBER RITZ: Beate Ritz, Epidemiology from UCLA.

PANEL MEMBER BLANC: Paul Blanc, Occupational and Environmental Medicine, UCSF.

PANEL MEMBER KLEINMAN: Mike Kleinman, Air Pollution Health Effects Lab at UC Irvine.

PANEL MEMBER MILLER: Lisa Miller, UC Davis, School of Veterinary Medicine.

PANEL MEMBER LANDOLPH: Joe Landolph, Departments of Molecular Microbiology and Immunology and Pathology and member of the USC Norris Comprehensive Cancer Center. I work in the molecular mechanisms of nickel, arsenic, chromium, and PAH carcinogenesis at the University of Southern California.

PANEL MEMBER GLANTZ: Stan Glantz, UC San Francisco. I run the Tobacco Center. And I'm in the biostatistics seat.

PANEL MEMBER HAMMOND: Kathy Hammond, University

of California, Berkeley, Environmental Health Sciences, School of Public Health.

PANEL MEMBER BESARATINIA: Good morning. I'm Ahmad Besaratinia from Preventive Medicine Department, University of Southern California, and I'm a cancer biologist.

CHAIRPERSON ANASTASIO: Great. Thank you, everyone. A few administrative items. Restrooms, drinking fountains are out the doors to your left. If there's a fire alarm, please exit down the stairs and proceed out the building. We have a very clean record on fire alarms, so let's hope we keep that up today.

(Laughter.)

CHAIRPERSON ANASTASIO: Two major items on the agenda today for this meeting. The first will be a review of the proposed cancer inhalation unit risk factors for cobalt and cobalt compounds. And the second is a review of the proposed updates to the chemical list in appendix A of AB 2588 air toxics hot spots emissions inventory criteria and guidelines regulations. So we'll do the cobalt before lunch, have a break for lunch in-house, and then we'll do the AB 2588 after lunch.

Which brings us -- oh, wait, sorry. One reminder, please when you're speaking, turn on your mic, get your face close to the microphone for our favorite

court reporter, Jim, will be making the transcript. And also people on the webcast it's difficult to hear if you're not speaking directly into your microphone.

Okay. Which brings us to major agenda item 1, our review of the proposed cancer inhalation unit risk factors for cobalt and cobalt compounds. So this document was from the Office of Environmental Health Hazard Assessment, which went through public review and comment during 2018. The document was revised and the Scientific Review Panel draft was sent to us to review. It was also posted on OEHHA's webpage for the public.

Today, we're going to hear a presentation first from OEHHA staff on the proposed cancer inhalation unit risk factors for cobalt and cobalt compounds. Then we'll have our Panel discussion and feedback we'd like to give to OEHHA staff. So I'm going to turn it over to John Budroe from OEHHA.

Take it away, John.

DR. BUDROE: Good morning. My name is Dr. John Budroe. I'm Chief of the Air Toxicology and Risk Assessment Section at OEHHA. I'd like to introduce Dr. Daryn Dodge. Dr. Dodge is the lead author on the cobalt cancer document and he'll be making the presentation today on both the document itself and response to public comments.

Dr. Dodge.

(Thereupon an overhead presentation was presented as follows.)

DR. DODGE: Thank you, Dr. Budroe.

Okay. I'm moving onto slide 1 here.

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DR. DODGE: Co -- elemental cobalt is number 27 on the periodic table. It's one of a number of transition metals. Transition metals, many of them, can generate reactive oxygen species in biological systems. And this is thought to be a major, if not the main, factor for its carcinogenic action.

Uses. There is a number of uses for cobalt. I list a few of them here. One of the major ones is cobalt meta powder is used as a alloying component in hard metal. Cobalt oxides and salts are used as pigments in glass and ceramics. And it's found as a component in lithium in nickel-based rechargeable batteries.

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DR. DODGE: And slide number 2, ambient air levels of cobalt. They're pretty low. Rural and wilderness areas of California you see levels of 0.0005 to 0.005 nanograms per cubic meter. However, levels in urban areas are relatively higher than that. In Southern California, mean levels you can find 1.3 to almost 9

nanograms per cubic meter with maximum levels. Highest levels measured is about 3 to 5.6 nanograms per cubic meter.

Now, I want to add here that under our Hot Spots Program, we're looking to avoid emissions from facilities that are blown offsite and into neighborhoods -- adjacent neighborhoods or where people work. So if a facility is emitting cobalt or any other pollutants, the concentrations at these neighborhoods immediately off the facility offsite location, the concentrations could be higher than what you're seeing here in this example for Southern California.

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PANEL MEMBER HAMMOND: Just as a question -- a clarification there. So what you're saying is those do not represent measurements around hot spots.

DR. DODGE: Yes, that's correct. Slide number 3, the bioaccessibility of the cobalt ion is considered in -- an important factor for carcinogenicity. The inhaled cobalt compound particles that are water soluble -- and for our purposes, for OEHHA's purposes, we're talking about greater than 100 milligrams per liter, will dissolve in the alveolar lining fluid and release cobalt ion there.

However, something different is going on with insoluble cobalt compounds, which we define as less than

or equal to 100 milligrams per liter. These water insoluble cobalt compounds will be inhaled and reach distal airways, alveoli, and be uptaken by pulmonary cells by endocytosis. They then dissolve intracellularly in the acidic environment of lysosomes. This process for insoluble cobalt compounds appears to be the reason why insoluble cobalt compounds have a greater cancer potency, which I'll get to later, that is compared to the soluble cobalt compounds.

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DR. DODGE: The next slide is number 4. This is just a list of a few of the commercially important cobalt compounds and their water Solubility. In the first row it's -- I show cobalt metal particles with a water solubility of 2.9 milligrams per liter. So that's well under our definition of water solubility, 100 milligrams per liter. Anything under that is considered insoluble.

The next two compounds are the sulfate and the chloride. And those -- that water solubility is considerably greater than 100 milligrams per liter. And the last two are the cobalt oxides and those are well under 100 milligrams per liter. In other words, our cutoff of 100 milligrams per liter as to whether a compound is considered soluble or insoluble works well for this sort of scheme.

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DR. DODGE: Next slide.

I'm now going to some of the toxicokinetics. There are a number of acute human studies, short-term studies. And what you see is a multiphasic elimination of inhaled cobalt metal, or oxides, from the lungs. The initial phase is a rapid phase. The half-life of -- is two to 44 hours. And that's primarily due to mucociliary clearance. And there's an intermediate phase of 10 to 78 days half-life. That's primarily due to macrophage-mediated clearance. And then there's a fraction of inhaled cobalt, which is retained long term on the order of months or even years. And that's due to what is thought to be cobalt bound to cellar components of the lung.

With short-term exposure, cobalt did not translocate or accumulate appreciably in other tissues with acute exposure. There are toxico -- next slide.

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DR. DODGE: There are toxicokinetic studies that look at long-term exposure. And this was performed by the National Toxicology Program, which I'll call NTP from now on. They conducted 13-week and two-year inhalation studies with cobalt metal dust in rats and mice.

Their main findings. Cobalt concentrations and

burdens in exposed rats and mice increased in lung and all other tissues examined, indicating absorption and systemic distribution occurs following inhalation.

Next point -- or next finding. Lung cobalt concentrations and burdens in rats and mice increased with increasing cobalt concentrations, but appeared to reach a steady state about day 26 into their 13-week and two-year studies. And finally, cobalt burden steadily decreased following cessation of cobalt exposure.

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DR. DODGE: Slide number 7. Continue on -- Continuing on with their findings. Cobalt concentrations in rats showed the following order: greatest in lung, followed by liver, kidney, femur, heart, serum, and lowest in blood. And these findings were similar in mice too.

Overall, normalized lung tissue burdens measured as a ratio of tissue burden to exposure concentration did not increase with increasing exposure.

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DR. DODGE: Next slide.

Now, we'll go on to the carcinogenicity of the cobalt compounds. The NTP performed an inhalation cancer bioassay in rats and mice for cobalt sulfate heptahydrate in 1998. Then they didn't -- they then followed up with a inhalation cancer bioassay in -- with cobalt metal dust in

2014. The carcinogenicity findings for cobalt metal dust will be used by OEHHA as the basis of the cancer potency factors for cobalt metal and all insoluble cobalt compounds. And this is for cobalt compounds with a water solubility less than -- less than or equal to 100 milligrams per liter.

The carcinogenicity findings for cobalt sulfate heptahydrate will be used by OEHHA as the basis of cancer potency factors for soluble cobalt compounds. These are -- again, this is for water solubility greater than 100 milligrams per liter.

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DR. DODGE: So these were two-year studies. For cobalt metal, they used F344/NTac rats and B6C3F1/N mice, 50 animals per exposure group per sex, per species. The concentrations were 0, 1.25, 2.5, 5 milligrams per cubic meter. Exposure duration was 6.2 hours per day, five days a week, for 105 weeks.

For the cobalt sulfate heptahydrate study, or assay, they used a slightly different strain of rats and mice, but the exposure groups were the same size, 50 animals per group, per sex, per species. Concentrations were a little lower in here, 0, 0.3, 1.0, and 3.0 milligrams per cubic meter. The exposure duration was the same in both studies. In other words, it was 6.2 hours

per day, five days a week, for 105 weeks.

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DR. DODGE: Slide number 10.

Let's go over the tumor incidence findings after two years of exposure to cobalt metal dust first in the rats. The main finding is increased lung tumor incidences in male and female rats, the alveolar/bronchiolar adenoma and carcinoma combined.

The results of the tumor incidence results you see a statistically significant increase in these types of tumors in all exposed groups 1.5, 2.5, and 5.0. And that's in both male and female rats.

In addition, there was a positive trend for this tumor type. In other words, as the dose goes up, you get an increase in tumors.

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DR. DODGE: Now, also in rats, you saw other types of tumors. In rats, you see an increase in adrenal medulla tumor incidences. This is -- specifically, this is benign and malignant pheochromocytoma. The increase was at the mid- and high-dose groups in both male and female rats. And there was a positive trend for this tumor type too.

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DR. DODGE: And there were still more types of

tumors found in rats. In male rats, there was an increase in pancreatic islet cell adenoma and carcinoma at the two highest dose levels. In female rats, you saw an increase in mononuclear ceel leukemia in all exposed groups.

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DR. DODGE: Now, let's talk about the tumor incidence data in mice. In both male and female mice, there was only one type of tumor found that had increased, and that was alveolar/bronchiolar adenoma and carcinoma, similar to what you saw in the rats. And as with the rat data, you saw an increase in these tumors in all exposed groups.

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DR. DODGE: Now, in the two-year cobalt sulfate heptahydrate assay, or study, the tumor incidence in rats you also saw an increase in lung tumors, although the response wasn't as strong. In male rats there was an increase in this tumor type at the high dose group of 3.0 milligrams per cubic meter. In female rats, there was an increase in the two highest dose groups.

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DR. DODGE: And the next slide here, you also saw an increase in pheochromocytoma as you did with rats in the cobalt metal study. However, this response again was not as strong. Female rats, you did see an increase in

this tumor type at the high dose group. But in male rats, the data was, what the NTP calls, equivocal evidence. You -- and that's because the increase was only seen in the mid-dose group, a statistically significant increase, but not at the high-dose group. And then there was no positive trend for this tumor type. So they gave it the equivocal evidence.

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DR. DODGE: Now, in mice, you -- again, there was an increase in lung tumors. In male mice, the increase was only observed in the high-dose group. And in female mice, it was in the two highest dose groups. And as with the cobalt metal data, you only saw an increase in tumors in the lung of mice. You didn't see it in any other organ system.

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DR. DODGE: So what other evidence is there for cancer from -- resulting from cobalt exposure?

There was only limited data for epidemiological studies. The best of which was by Sauni et al. in 2017. And this was a retrospective study at a Finnish cobalt plant. The N was 995, which is pretty high for an epi study, but this included all employees that worked at the plant for at least one year or more. They did have a mean follow up of 26.2 years.

The airborne cobalt concentrations at the plant, it mostly was as the sulfate or metal dust. They measured several times per year. Concentrations ranged from 0.1 to less than 0.02 milligrams per cubic meter. What they were -- the workers were exposed to really depended on the job top type or department they were in at the facility.

The results were that they saw no increase in cancer risk with five years of employment at the facility. And this was based on a standardized incidence ratio, or SIR. The so-called control group was a regional Finnish cancer database. An SIR of 1.08 for a total cancer risk suggests they were no different than the control group or not much difference in total cancer risk. What's interesting here is that for the workers, the SIR was 0.52. And that was specifically for lung cancer. And this would suggest that the workers actually had less lung cancer than the control group.

The authors couldn't explain it, because there was no difference in smoking. They kind of just left it at that.

There were some issues with this study. They noted that -- the authors noted that there was respirators available, but not mandatory to use, so it was unclear from the study how often the workers were using these respirators. So we don't actually know what the true

exposures were in many of these workers.

They didn't have a mean exposure time for the group of workers either. They only presented data as employed at the plant for at least one year or for five years.

DR. BUDROE: Dr. Hammond, I think you had a question.

PANEL MEMBER HAMMOND: Yes. Thank you. This is good. Yeah. My -- I think I know the answer, but I'll ask it anyway. The question is did they do an analysis by milligram per cubic meter years of exposure? I mean, you're saying that clearly there was a difference by the jobs in the exposures. And in many facilities, 90 percent of the workers might have low or no exposure. And so looking just at that -- all workers compared to the neighboring area might not have any meaning, unless they've at least categorized the jobs or some milligram per cubic meter individual years. Are they -- did they do that?

DR. DODGE: I'm pretty sure they didn't present the data as milligrams per cubic meter years.

PANEL MEMBER HAMMOND: They did?

DR. DODGE: They did not.

PANEL MEMBER HAMMOND: Yeah. I mean so I think it's -- one has to be careful how much we can deduce from

the study --

DR. DODGE: Correct, yeah.

PANEL MEMBER HAMMOND: -- if we don't know what percentage of people had any kind of significant exposure.

PANEL MEMBER RITZ: I actually think I know why they don't see anything and why they see such weird numbers. All you have to do is look at the table 1 and you see that the bulk of their workers were between 15 and 29 years when they were employed. So how many years do we have to wait before we see lung cancer or any other? Twenty-six years isn't enough.

PANEL MEMBER HAMMOND: This isn't --

PANEL MEMBER RITZ: Yeah, but still, you know, if most people are around 22 or 3.

PANEL MEMBER HAMMOND: Yeah, that's back to like the diesel study going back many decades, where ten years after exposure you saw nothing. You had to be at least 20 years out. So I think it's important. You're right to point all these out, yeah.

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DR. DODGE: Okay. I'm moving on to the next slide. Other evidence of cancer due to cobalt exposure comes from genotoxicity studies. There was a considerable database of genotox studies for soluble cobalt compounds and cobalt oxide compounds.

So this includes the DNA damage assay, or comet assays, oxidative DNA damage assay, in vivo DNA adduct assay, bacterial mammalian gene mutation assays, chromosomal aberration assay, and the micronucleus assay.

Now, these were mostly positive findings for genotoxicity, among all these assays. With the exception of the bacterial and mammalian gene mutation assays, those are primarily equivocal or negative.

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DR. DODGE: There are a few genotox studies for cobalt metal dust, where they looked at DNA damage assay, or comet assay, in vivo oxidative DNA damage assay, gene mutation analysis, bacterial and mammalian gene mutation assays, chromosomal aberration assay.

Positive genotox findings included results from the comet assay, oxidative DNA damage, and gene mutation analysis. And again, there wasn't a lot of positive results from bacterial and mammalian gene mutation assays.

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DR. DODGE: Next slide.

So overall the cancer hazard evaluation here based on lifetime NTP inhalation studies for both the cobalt metal and the sulfate heptahydrate, cobalt is carcinogenic in multiple species, rat -- that includes rats and mice. Cobalt induced lung tumors that were of

the same histogenic type in both species. Cobalt induced tumors at one or more sites in both rats and mice. In addition, there was numerous positive genotoxicity studies. Combined, these factors point to a strong potential for cobalt to induce tumors in humans as well.

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DR. DODGE: And next slide.

Now, I'll go into the cancer slope factor derivation. The first step in the cancer slope factor, or CSF, derivation is converting the NTP tumor incidence into what's called the effective tumor incidence.

The effective tumor incidence is the number of tumor-bearing animals over the number of animals alive at time of first occurrence of the tumor. This removes animals from the assessment that died before they are considered at risk for tumor development.

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DR. DODGE: Now, I just give this table as an example. This is a comparison of the NTP tumor incidence with the effective tumor incidence for rodents exposed to cobalt metal dust. So the NTP tumor incidence is the second column from the right. In the denominator you see 50 animals per exposure group. Well, at least in most cases. Sometimes, it's less than 50, because an animal died due to some accident that had nothing to do with the

exposures. So they reduce it to like 49 rather than 50.

And then the effective tumor incidence is the far right-hand column. You see that the denominator often is less than 50. It's reduced by two or three animals in most cases. And so it reduces it a little bit. What this gives you an indication of is that at least with regard to these types of lung tumors, they were showing up early, like in the first year of exposure in this study, so not many animals died prior to the appearance of the -- of this tumor type.

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DR. DODGE: Next slide.

So now we have the effective tumor incidence. We also need to convert the air concentrations to an average daily dose and that's in milligrams per kilogram body weight per day. So this equation is shown here. Dose is equal to inhalation rate times concentration over body weight. Concentration is time adjusted to an annual average. The exposures were 6.2 hours per day. So this is 6.2 over 24 hours. Exposures are five days a week. So this is five days over seven days. Body weight is used. It's an average over the two-year exposures. The NTP measured body weight on a weekly basis during the first year of the exposure and about every two to four weeks during the second year of the exposures. So that's the --

how the average was determined -- average body weight.

The inhalation rate is based on the body weight of the animal. Body weight -- there's a good relationship between body weight of rodents and its inhalation rate. So we have these equations down here at the bottom next to the bullets, one for rats and one for mice. So this is -- we use these equations to determine the inhalation rate based on body weight of the animals.

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DR. DODGE: So using the dose equation here, we converted the chamber -- cobalt metal chamber concentrations to an average daily dose. And this table just shows what the average daily doses we used for the rats and mice.

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DR. DODGE: So now we have the fraction affected, the effective tumor incidence and the dose. So now we can run the multistage cancer model in the Benchmark Dose Software -- U.S. EPA's Benchmark Dose Software to determine the cancer potency. Potency values derived using the bench -- we derived potency values based on a benchmark response, or BMR, response rate of five percent to calculate a benchmark dose. The 95 percent lower confidence bound on the BMD, or benchmark dose, is used to calculate the cancer potency.

So the cancer slope factor, what we're looking for here is simply five percent, or 0.05, over the BMDL, which is the 95 percent lower confidence bound on the BMD.

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DR. DODGE: We determined cancer slope factors from all the tumor types that were found, individual tumors. This included the lung tumors in all rats and mice, both males and females. As you may recall, the -- we saw pheochromocytoma in male and female rats. Rats also -- or male rats also had an increase in the pancreatic islet cell adenoma and carcinoma. And you saw leukemia increase in female rats. So we developed cancer slope factors or individual cancer slope factors for all these tumor types.

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DR. DODGE: So plugging the info -- the data into the Benchmark Dose, or BMDS, Software, using the multi-stage cancer model, we get a plot fit to the data. In this example, this is the lung tumors in male mice exposed to cobalt metal. So what we have on the X axis is the average daily dose, which I showed you how we calculated earlier -- an earlier slide. And the fraction affected is the Y axis and that's the effective tumor incidence there, which I showed you how we came up with in an earlier slide.

So the data points are shown in green with the error bars. In the lower left-hand corner, that's the control group. In the -- as you go up and to the right, you get your low-dose group, mid-dose group, and your high-dose group at the upper right-hand corner there. The Benchmark Dose Software fits a line to that data, which is shown in red.

Now, we also plugged into the model that we wanted the benchmark response rate of five percent. In other words, we want to define the response -- five percent response rate, the increase in this particular tumor type, over the control group of five percent.

The benchmark response rate gives us a BMD, or benchmark dose. That's the vertical black line in the lower left-hand part of the graph. It's right next to the BMDL, so it looks like one solid line to me from here. But anyway, they were very close together in this particular graph, the BMD and the BMDL.

So the dose, or average daily dose, that you get at that BMDL where it intersects the X axis, that gives you a dose. And I believe it's around 0.01 -- 0.011 milligrams per kilogram per day. The cancer slope factor is basically just 0.05 over the BMDL of 0.011 milligrams per kilogram day.

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DR. DODGE: Now, before I go on -- let's see. Okay. Well, rats developed tumors in more than one organ system. So before I go on to show you more of the cancer slope factors we devised, we got a note that rats developed tumors in more than one organ system. And basing cancer risk on only one tumor type may underestimate the tumor risk.

So we did what's -- we used what we call the MS Combo Model in U.S. EPA to come up with multi-site tumor cancer slope factors. This come -- we used the model to combine the lung, adrenal, medulla, and pancreatic islet tumors combined for male rats. And in female rats, it was -- we combined leukemia, lung, and adrenal medulla tumors.

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DR. DODGE: Now, the final calculation we need to do is to extrapolate to humans, because this is rodent data. So we take the animal cancer slope factor we came up with and go to extrapolate to cancer slope factor human equivalents. And this is used -- this is done by using body weight -- scaling body weight to the 3/4th power. And this equation is shown here in the middle of the slide. The human cancer slope factor is equal to the animal cancer slope factor times the body weight of the human or the body weight of the animal to the 1/4th power.

This interspecies scaling factor is used to account for pharmacokinetic differences, as well as for pharmacodynamic considerations.

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DR. DODGE: Now, in this table, this is the major findings of cancer slope factor for each male and female rat and mouse. So in male rats, we -- the highest cancer slope factor we got was, of course, when we combined the various tumors found in male rats. And the cancer slope factor -- the human cancer slope factor is the column on the far right. It was 22.17 milligrams per kilogram day to the minus 1.

For female rats, we combined the tumors found in female rats and we came up with 10.7. Male mice, as you recall, tumors were only found in the lung. However, it was a pretty strong response. And that actually resulted in the highest cancer slope factor of 27.49. So among male and female rats, male and female mice, the most sensitive species here is mice, the most sensitive sex is males. So this cancer slope factor is what we use to represent the cancer -- cancer risk from cobalt metal.

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DR. DODGE: However, there was a bit of a hitch here. U.S. EPA came out with the updated version of their benchmark dose software after we first came out with this

data, this analysis. In their software, they actually gave recommendations as to the BMR, or benchmark response, that is used in their model.

Now, I'm showing this graph from -- I showed you this graph several slides ago. This is again the lung tumors in male mice. The Benchmark Dose Software, it shows the data there for control, low, mid, and, high dose. And then the line that was -- the plot fit or the line fit to that data resulting in a BMD and BMDL at the lower left hand.

So the new version of the software now gives recommendations as to the BMR. In this new software update, a five percent BMR resulted in what's called a questionable recommendation. This is because the BMR chosen was three-fold lower than the lowest non-zero dose, and the BMDL was 10-fold lower than the non-zero dose.

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DR. DODGE: So what we did is --

PANEL MEMBER BLANC: Can you repeat that?

DR. DODGE: Okay. I can try to repeat that.

The new Benchmark Dose Software that U.S. EPA came out, a new version, a new update now has recommendations as to how the benchmark response is fit to the line, whether it's an adequate fit, questionable, or unusable. They didn't do this before. They just kind of

left it open.

So what they're saying here is that a five percent response rate plugged into their software results in a questionable recommendation, because a five percent response rate is outside of their -- is beyond the area of -- I forget what the term is, but's it just too far away from the lowest non-zero dose. If you -- the lowest --

DR. BUDROE: The -- essentially what the software has concerns about the BMDL being out -- too far outside the range of observable data.

PANEL MEMBER HAMMOND: But, you know, I -- it's --

PANEL MEMBER KLEINMAN: But that is really a function of the fact that you had very positive results even at the lowest dose. So I don't -- you know, yes, it's outside of strict guidelines, but you're dealing with something that has a very steep onset curve.

DR. BUDROE: Correct.

PANEL MEMBER HAMMOND: That was exactly my point -- Kathy Hammond -- that you're -- all the doses were over 80 percent of the animals. I mean, I remember there was like 47 or 48 of the 50, you know, got cancer. So I think it's important to think of what -- to be clear what's questionable. There's no question that it's

causing cancer. It isn't as potent. The question is just what is the dose where you get a five percent increased risk. And certainly, it's really hard to calculate that given that kind of response. But I think it's important to be clear, there's no question about the cancer risk.

PANEL MEMBER GLANTZ: Go ahead.

PANEL MEMBER RITZ: I find that very suspicious that a software package is giving a qualitative statement about data. Isn't that something that experts like us should be deciding?

DR. BUDROE: That's what I guess the editorial judgment that U.S. EPA chose to make.

PANEL MEMBER GLANTZ: Well, I met with the -- well, I met -- I mean, you guys have stolen my punch line.

PANEL MEMBER HAMMOND: Yeah, let the biostatistician speak.

PANEL MEMBER GLANTZ: So I met with them yesterday to talk about this. And I think that -- I agree with you, I mean, this software is making an arbitrary decision that's stupid. And I think it should be ignored. And, I mean, if you look -- if -- mean they're right that the lowest exposed group is quite lot higher than zero, so there is that big gap. But you do have a zero exposure control group too. So your -- the estimate is not outside of the range of the data.

And as Mike said, I mean, if you look at this graph, probably it's underestimating the slope of the curve at low doses, so that it's probably way underestimating the actual cancer potency at the bottom. Now, the problem is you don't have any data down there and so you don't know. But I mean my recommendation is that this -- that they just stick with the 0.05 estimate coming out of the program, say that there's uncertainty here, because there's that -- you know, they didn't expose any animals down, you know, with a low -- you know, a low exposure, but that they should -- that whole thing about the software is unhappy should just be dropped out of the report. You should use what it came up with, but then put a strong statement in that that almost certainly is underestimating the cancer potency at low doses, I mean, for exactly the reason that Mike said.

So this isn't -- by the way, in the cadmium -- or pardon me, cobalt sulfate thing, this isn't a problem there, because they have data down at the low -- you know, they have data where rats were exposed at lower levels. But I found that that was all very confusing to me. And I think what they did is -- I mean, it's not, you know, as a general principle, a bad thing to say it would have been nice to have had more data at lower exposures. But I think some software programmer programmed that, that's not

a reason to make policy here.

And I think we need to strongly say this is probably underestimating the risk. I think it's the best you could do with the data you have, because if you start coming up with some alternative formulation for the shape of the curve, which is, you know, what you would need to do, that's going to be arbitrary too. So I think using the standard protocol that you did to fit the curve is fine.

But anyway. But I think you have like one, two, three, four people who all independently came up with the same conclusion, which is pretty strong.

PANEL MEMBER BLANC: Paul Blanc. But there actually could be other sensitivity analyses you could do with the data that you have that might reassure you about the dynamics or shape of this dose response. And two thoughts that come to mind immediately. One is that since you're not looking at multi-site cancers with the mice, but only looking at the lung cancer relationship, that's correct, I understand

DR. DODGE: Correct.

PANEL MEMBER BLANC: For comparison -- comparative purposes, it might be helpful to see what your dose response looks like for lung cancer only in the rats, since biologically they should be behaving similarly.

That's one thing. Because the -- you make the argument that on general principles, multiple cancers should be combined as the endpoint, because that will be more sensitive.

But I'm not sure that that's what your data would show. And secondly, there is a phenomenon here where the data for actual lung cancer and not lung cancer plus lung adenoma are cleaner, in that there's no spontaneous lung cancer in the control rodents, at least in the rats. It's zero, right?

DR. DODGE: I think you're correct. Yeah, the rats may have not had as much --

PANEL MEMBER BLANC: Right.

DR. DODGE: -- of the spontaneous tumors as the mice did.

PANEL MEMBER BLANC: So again, perhaps not as your main analysis, but as your way of looking at the -- how the data performed, you may find that your estimate has less issues with it if you actually look at the cancer, even though you make the argument that it's more sensitive to combine the cancer and the aden -- the non-malignant tumors of the lung.

I don't know if that would be the case, but I could imagine, looking at different scenarios as a way of saying, look, this is all going in the same direction.

There's not an order of magnitude difference between the estimates we're getting for the cancer slope. And that might reassure you that some of the challenges you're facing with this steep takeoff are -- can be discounted.

I'm not sure that would be the case, but it would be -- it potentially might be worth you looking at that. Also, by the way, is it such a violation to combine the male and the female rats, and the male and the female mice? Because they're all behaving the same way, it seems like you're greatly reducing your power to make an accurate estimate by --

PANEL MEMBER GLANTZ: Yeah. You know, but the problem they -- I mean, that's all reasonable. But the problem they have is that this -- like, if you go back to slide 19 -- or 10 rather. So -- so if you look -- if you look at the -- at the tumor incidence between zero and the lowest dose, it goes from 2 to 25.

PANEL MEMBER BLANC: But it doesn't --

PANEL MEMBER GLANTZ: Well, this is just the lung cancer.

PANEL MEMBER BLANC: This is both the adenoma and the carcinoma. That was actually my point about all --

PANEL MEMBER GLANTZ: Oh.

PANEL MEMBER BLANC: -- what -- when you look at the carcinoma, which is in the main document, I don't know

what page, but --

PANEL MEMBER GLANTZ: So if you go to 14. So what's 14, is that the one you said Kathy?

PANEL MEMBER KLEINMAN: Page 55.

PANEL MEMBER GLANTZ: So that's 15.

PANEL MEMBER HAMMOND: Oh, these are sulfate. You want to do metal, don't you?

PANEL MEMBER BLANC: I think it's in the main document, not in the slides.

PANEL MEMBER GLANTZ: Well, 13.

PANEL MEMBER KLEINMAN: Page 55 in the main document.

PANEL MEMBER HAMMOND: I think just to say I think kind of what we're thinking about, if I'm understanding my colleagues, but that it may be that because there's this high background level that we're starting with 16 out of 50 in the group that you're using for analysis, it might be that if you were to use another species, it might be worthwhile seeing. I mean, I think that we could come away from what you've shown to say -- originally, we're starting this that whatever estimate we have has a high risk of being not sufficiently protective, that we've underestimated the potency, as you've said. But it might be worth trying to check the potency with the rats as opposed to the mice, because there's less of that

background, and therefore may be less of that error.

And then if it shows a -- it may not show as low a number. If it doesn't, we know that the mice are more compelling then. But it might give us better information. I guess I would love to just see what that came out to, if you did the dose response for the rats, male rats as opposed to the male mice. The male rats having the background zero dose of two as opposed to 16 out of 50.

I can't look at this and know how it will come out. I'm sorry.

DR. DODGE: Oh. Remember, we adjusted the inhalation rates based on the body weights of the animals. And we used two different equations for rats and mice. We update -- OEHHA, our agency, updated that information, because we have a lot more recent data on the body weight relationship to inhalation rates. We got a much -- I think we did a good job in coming up with a better equation than what was used, which was, you know, 30 years, 35 years old.

We only had -- we only had time to do that for the rats. That had a -- quite an effect on the cancer slope factor though, because we had used Anderson 1983 equation for rats.

So that caused a difference, because for mice we used the old equation. That's all we had at the time. We

also have to take into account where extrapolating to humans from a smaller animal from mouse. So you get a larger difference in -- larger increase in the cancer slope factor. So I understand what you're saying just looking at incidence rates, how it looks like the rats should have a bigger response. But in our extrapolation from inhalation rate, yeah, it does affect it. Makes it look like the mice are much more sensitive than they truly are.

PANEL MEMBER GLANTZ: Yeah, but -- and then I'll stop and give Joe a chance. But that -- none of this though is going to deal with the problem that your lowest positive exposure is a lot high -- you have a big response in all of the data at the lowest expose -- non-zero exposure they looked at.

And so you don't have any direct data with which to estimate the curvature of the line between zero and that dose. And the slope is depend -- very dependent -- I mean, it's near zero is going to heavily depend on that. So I think that you're just kind of stuck unless somebody goes and gets some more data.

But it's very clear I think that the -- I mean, I think you should do it the way you did it, but I think we need to be -- just say that you are almost certainly underestimating the potency. Like, if you took -- if you

took the data, if you -- just for kicks -- I mean, somebody suggested a sensitivity analysis. And if you just go back to the slide with the curve on it. You know one thing you could try, just for kicks, is to fit that with a saturating exponential. And you're going to get a really steep slope at the low levels. But the problem is is that that slope is effectively going to be determined by the upper doses where there's not that much difference. So that's going -- it will be a much bigger slope, but it's also going to be kind of unreliable too. So I think you have -- the problem is you just don't have data to fill in that hole. I'll be quiet.

PANEL MEMBER RITZ: So being an epidemiologist, we usually would not estimate this in a cohort according to the lifetime rate, but something like a Cox model time to event. And I heard you saying that these mice or rats actually got their tumors early. That's why nobody else died, right?

So given that they got their tumors early, they had no time to -- those -- and almost every one of these animals developed a lung cancer, we really don't know what's happening at lower doses when they don't develop lung cancer that kills them off in terms of other organs.

So I would actually be quite concerned that there might be effects on other organs that we're just not

seeing because they would be showing effects later. One comes to mind, because the alveolar clearance here, where does that go, the mucous? It gets swallowed, right? So it goes in the GI tract.

Also, these mice and rats probably lick themselves and aerosolized exposures are on the -- on the fur. So I actually would really like to see it, but I know we don't have them, but I would like to see lower dose studies and other organ systems.

DR. BUDROE: Yeah. I think part of the problem here is when NTP did the cobalt metal study, they were looking back at the cobalt sulfate study and thinking, well, cobalt metals can be less potent, and they wound up with a big surprise. I mean, they essentially said in the document they were surprised. So that's where part of the problem is coming from, but it's really not likely that anybody else is going to repeat this study. I mean, NTP is one of the few people that are -- if only doing the inhalation cancer studies these days.

PANEL MEMBER LANDOLPH: Yeah, a couple comments.

First, thank you for all your work. It's a huge amount of work, and I appreciate it.

In looking at that curve -- in looking at that curve that you have up there, I mean, one of the questions -- a couple questions occurred to me. One is,

is it linear from zero up to some dose? And then does it saturate -- as a response saturating for some reason? Or the other one is, is it a different function entirely than a linear that saturates in it. That's -- I would discuss that concisely in your report, so that you let people know we -- we're a little bit curious about that shape of the curve.

The other thing is the -- when I was reviewing this, the whole thing sounds a lot like nickel carcinogenesis to me. There's tremendous parallel between the two. I've worked on nickel carcinogenesis since 1983. And the insoluble nickel compounds are -- we call them phagocytosed the particles from 1 micron up to 10, or something like that.

And because when you phagocytose these particles, you can see them under the light microscope, you get a real bolus of nickel into the cell. So if it were all to dissolve, it would be millimolar, and sometimes the cells pop from osmotic shock.

And this sounds very much like that. And the -- the insoluble compounds are much, much more toxic and more carcinogenic than the soluble ones. The soluble ones really not are very -- are not very carcinogenic at all, because you get the bolus into the cell by phagocytosis.

And then the same -- the other point - it's very

interesting. I was reading this - that there's some thought about oxygen radical generation, which has gradually been creeping up over the years, but not a lot of real certainty about mutagenesis. And it turns out with nickel - we're getting ready to publish a paper now - the nickel is not positive in any of the classical mutagenesis assays for a mutation while being resistance to mutation 6-thioguanine resistance.

But we hit a home run, we sequenced the whole genome of the nickel transformed cells. And guess what, there's all kinds of chromosome amplifications and deletions, and there's point mutations all over the place. So there's something interesting going on with these oxygen radical generating agents, like nickel and like this cobalt that still needs to be ferreted out. It seems very interesting.

DR. DODGE: Yeah, there's similar studies with cobalt showing that particles are phagocytosed and result in up to millimolar concentrations within cells. Yes, it's very similar to nickel.

PANEL MEMBER GLANTZ: So just before you go on, we've had this big discussion, I mean I think -- can we -- you know, I know we usually make recommendations at the end, but we just finished talking about this. And I'd like to suggest -- I don't know if I want to -- I'll move

it, so we can do something, that you delete that discussion of the software telling you what to think and just go -- stick with the -- just the conventional analysis, but highlight the fact that because of these data problems, they're almost underestimating the cancer potency.

I don't know how much, but you're almost certainly unestimating it. So I'd like to move that we recommend they do that. Is that okay?

CHAIRPERSON ANASTASIO: Well, let me address that for a second. I think you're going to talk in the next couple of slides about your alternative approach, right, which ended up giving a slightly more protective value, a slightly higher cancer slope factor?

DR. DODGE: Yes.

CHAIRPERSON ANASTASIO: So it seems to me that we'd rather go with the slightly higher cancer slope factor.

PANEL MEMBER GLANTZ: Okay. We can wait. Okay. I'll withdraw what I said. But I'll tell you, the problem I have with that is that essentially what they did, if you look in the appendix, is they have the formula -- the equation for the line and then they -- they differentiate it to get a slope, but then they -- they use the parameters from that fit in the calculation. So all of

the uncertainties and problems that are associated with the fact that there's no data down -- you know, between zero and the first point are still embedded in that other calculation.

So I actually think it's kind of misleading to say that's somehow better, you know, because it's based on the same information. It's just sort of making a couple of different assumptions, which I think are pretty arbitrary. And, you know, basically, the 15 percent number that that's -- rather than using a five percent over the background, they're using 15. But, I mean, as best as I can tell, that was just picked to get it up high enough that the computer program wouldn't complain, which I think is not a good reason.

But I'll withdraw my suggestion. But I -- I hate that other analysis, because I think it just look -- it's trying to look different. But every single problem that we've talked about so far with this is just -- it's in the other analysis too. It's just more obscure.

PANEL MEMBER KLEINMAN: One other point. In your an inhalation dose calculation, it looked to me like you're assuming 100 percent deposition. You don't take into account that not 100 percent of the particles will actually deposit in the respiratory tract.

DR. BUDROE: That is a health protective

assumption, correct.

PANEL MEMBER KLEINMAN: But in this case, I don't think it's health protective, in that you're calculating your slopes based on a higher dose than actually is. The effects you're seeing are most likely due to a lower inhaled dose.

DR. BUDROE: I get to where you're going with that. It's -- the problem is trying to adapt. For example, one of the -- for example, the multi-path particle dosimetry software trying to adapt that to what we're doing, and nobody has really gotten to that point yet. U.S. EPA is not even doing it with all their squads of particle dosimetry people.

PANEL MEMBER KLEINMAN: Yeah. No, I'm just amplifying what Stan just said.

DR. BUDROE: Right.

PANEL MEMBER KLEINMAN: You are coming in with a less than conservative actual proposal. So in all likelihood, you know, even though you're getting, you know, a -- you know, and you will be having a slightly bigger slope factor. This, in all likelihood, does not overestimate the risk. If anything, it's underestimating potential risk.

DR. BUDROE: Agreed.

PANEL MEMBER KLEINMAN: And I think, you know,

that should be made very clear.

PANEL MEMBER HAMMOND: Yeah. I just would like to say -- Kathy Hammond -- I agree as well. And I think it's very important that we -- we make that point that where there are problems in the data - and they're not you're problems. They're the problems with the experiments - that the errors that they lead to are all errors which underestimate the potency, because it -- there's an underlying assumption of 100 percent deposition, which overestimates the dose, therefore the effective dose -- without knowing how much it's doing it, the effective dose is actually a lower number, following Michael's comments.

And similarly, we've got the dose -- the -- I don't actually agree with Stan in taking away the designation of questionable. Because the software tells you that, I think we need to be honest and up front with that, but I think we just need to then, after that, say what's questionable is it could well be that this is underestimating the potency, not that -- there's no question whatsoever about the carcinogenicity.

And I think it's just -- it's very unfortunate NTP didn't look at their data and say oh, my golly, time to do another study at lower doses.

PANEL MEMBER LANDOLPH: Yeah. Of course, the

problem -- the problems of getting more low-dose data are well known. You start getting into the mega-mouse experiment that Liane Russell did at Oak Ridge Laboratory. We're using thousands of mice to get it. So you're having intrinsic difficulties addressing that.

But, you know, Was looking at this curve. And if you almost took zero in the first two points, you might get a better estimate of the slope. This curve -- the slope is changing at every point clearly. And I think you should discuss that, as best you can. You can't fix it at this point, unless somebody comes up with a new theoretical construct.

PANEL MEMBER GLANTZ: That might be a better way to do it.

PANEL MEMBER LANDOLPH: If you can do it.

PANEL MEMBER GLANTZ: Well, just --

PANEL MEMBER HAMMOND: Just do a straight line.

PANEL MEMBER GLANTZ: -- just do a straight line. That's probably better.

PANEL MEMBER HAMMOND: Well, I was looking at that.

PANEL MEMBER LANDOLPH: With zero in the first two points. Yeah, I think that would be more accurate. Just tell people why you're doing it.

CHAIRPERSON ANASTASIO: Thoughts about that idea.

OEHHA.

DR. BUDROE: We would have to -- I mean, we prefer to use all the data -- all the data we have. You know, we'll drop high doses, if necessary, if we can't get a good fit. But if we can get a fit, we prefer --

PANEL MEMBER GLANTZ: Well, no, I mean, you -- that gets back to the con -- I mean, I agree with Kathy. We could leave the questionable thing in there and it would say. But the thing that makes it questionable is that you're underestimating the dose. But actually, you know, it may be if you're interest in getting something that's, you know, closer to reality, drawing the straight line between the first two points. I mean, I just drew the line. It's probably not going to make a huge difference actually.

But that might be a way to like do a little bit of a sensitivity analysis or something. If you just do a straight line between the first two points, and -- but it's clearly -- the questionable thing about the fit is that you're underestimating the slope at the low doses. There's just no question about that.

And, in fact, if you look at the residuals, you can see that you're below that -- the first non-zero point, the fifth is way below that, which is more evidence that you're underestimating the slope at low levels. I

mean, whether based on the biology, there would be something you could say is, well, here's the slope we've got. We're going to increase it by a factor of something or another to compensate for all these problems. I don't know if that -- we could come up with something that would be defendable.

But, you know, it's just clear that -- and again, I don't think that the slope -- the thing you did next solves the problem. It just obscures it.

PANEL MEMBER RITZ: So this is a parametric model, right? You could just use a spline with a node at the first point to estimate that, instead of, you know, anything else.

PANEL MEMBER HAMMOND: Then it would be a straight line.

PANEL MEMBER RITZ: Yeah.

CHAIRPERSON ANASTASIO: Daryn, do you want to tell us about the approach that Stan hates.

DR. DODGE: Well, okay.

(Laughter.)

DR. DODGE: All right. So we're going on to the next slide here. So, what we were -- what we're -- what we were proposing was that if a BMR of five percent, for example, yields a questionable cancer slope factor, we would use what's called the exact formula for the

calculation of the cancer slope factor. And we give this equation here. It's the cancer slope factor is equal to the minus natural log of one minus BMR over the BMDL.

So this estimate is derived by solving for the beta parameter in the risk equation and inserting the result into the log-likelihood equation for beta to use it to profile the BMD and obtain the BMDL.

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DR. DODGE: So the next slide, what we -- when we applied the exact formula, we get a constant BMD over a range of BMRs. From five to 15 percent we got the same BMD. This exact formula appropriately accounts for the increased curvature of the dose response relationship at higher dose levels and BMRs.

Again, what I should note here is that in the final bullet that BMR 15 percent gave a viable response in the Benchmark Dose Software. So five percent gave a questionable, but we only had to bump it up to 15 percent to get a viable. That's because the BMDL is now within ten-fold of the lowest non-zero dose. So I'm just explaining the U.S. EPA software.

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DR. DODGE: So a different -- the benchmark dose or the -- I should say the cancer slope factor that results from going from five to 15 percent in order to get

a viable response really doesn't change much. The cancer slope factor that is doesn't change that much.

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DR. DODGE: So we're -- that's what we're showing in this next table. So the U.S. EPA software -- Benchmark Dose Software their results are kind of in the middle columns there. The cancer slope factors are in bold, and the CSF column, and next to it is their recommendation.

So at a five percent response rate, you get a cancer slope factor that's questionable. If you go down to the next row, a benchmark response rate of 10 percent is also questionable. Then you get down to a BMR 15 of percent and it's called viable and recommended.

The cancer slope factor doesn't change all that much. It goes from 4.46 to 4.22. Now, in the far right-hand column, that's where we applied the exact formula. And you'll see from a BMR of five percent to 15 percent, it gave the same cancer slope factor of 4.57 milligrams per kilogram day to the minus one. So that's what we proposed using.

DR. BUDROE: And kind of to put this into perspective is what you're talking about is a change in the potency factor of like five percent. You know, we're a long way from order of magnitude differences. So we're kind of fine-tuning this. But in real-world terms, these

numbers are all falling out to be about the same.

PANEL MEMBER GLANTZ: Yeah. Well, see, that's another reason to like not do it.

(Laughter.)

PANEL MEMBER GLANTZ: Because there's nothing -- you're pulling 15 -- basically, you picked 15 percent so the program wouldn't complain, but that doesn't fundamentally change the data or the problem that you've got. And so I -- I just think you should go with the -- they're all 4.5, you know, or less, and -- anyway, I'll stop obsessing. But four of us had the same exact view of reading this inde -- without talking to each other.

PANEL MEMBER LANDOLPH: And, you know, it would make me happier if you just did a simple linear least squares fit to the zero point and the first two data points, and just put it in the document and say this is a comparison of what we do, what we get no matter what we do through these three different techniques just as a check.

DR. DODGE: Sure. We can -- we can add that, yeah.

PANEL MEMBER LANDOLPH: Yeah, that shouldn't be too much work I don't -- I hope.

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DR. DODGE: Okay. I'll go on to the next slide here.

PANEL MEMBER GLANTZ: One point. By first two data points, you mean the zero and the first non-zero?

PANEL MEMBER LANDOLPH: First two, yeah.

PANEL MEMBER GLANTZ: Right.

PANEL MEMBER LANDOLPH: So the zero point and first two real --

PANEL MEMBER GLANTZ: Well, I wouldn't use the first two, I would just -- because that's going to again underestimate.

PANEL MEMBER HAMMOND: The first one is the same. They're the same Y value.

PANEL MEMBER GLANTZ: Yeah. But X values are very different. So you're going to -- that's --

PANEL MEMBER HAMMOND: That's what I'm trying to say.

PANEL MEMBER GLANTZ: Yeah, so that's going to give you a lower slope on that.

PANEL MEMBER LANDOLPH: Yeah.

PANEL MEMBER GLANTZ: So, I mean, I think if any -- if you want to do it, I would just use zero and the first point.

PANEL MEMBER LANDOLPH: Yeah, I hear what you're saying. I'm thinking that the low-dose points are also not so accurate, you know, because they're smaller, and you have big error bars and all that. So it's kind of a

compromise. Do it both ways and just report what you got.

PANEL MEMBER GLANTZ: I don't like that either. I think you should just go with the standard approach and say we -- the software highlighted a problem that there's a lot of uncertainty, but the -- one thing we're pretty confident of is the uncertainty is all in the direction of underestimating the risk. You know, it's not questionable in that you're overestimating the risk. It's questionable that you're underestimating the risk.

DR. DODGE: Okay. So I'll go back to this slide, it looks like, 36. Well, using the exact formula, we come up with a cancer slope factor of 28 milligrams per kilogram day to the minus one. That's all I'm showing here in this slide the extrapolation to the human cancer slope factor.

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DR. DODGE: Next slide.

So -- okay. That was just for cobalt metal. We also did a derivation for cobalt sulfate heptahydrate. So we developed cancer slope factors for the lung tumors, for pheochromocytoma. It was in female rats only.

Then we also did a multi-site tumor cancer slope factor combining the lung and adrenal medulla tumors that occurred in female rats.

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DR. DODGE: So this will go a little faster, because I went into more detail with the metal. We don't have to do so with the sulfate here.

Of course, we have to determine the effective tumor incidence. And so that's just a comparison here for -- in female rats, the pheochromocytoma in the lung tumors.

NTP tumor incidence is the column second from the right. Again, it's 50 animals per group unless some animal died early in the study from an accident. And it died -- basically, died from some cause not having to do with the exposures. And the effective tumor incidence is over there in the right-hand column.

You might notice that these numbers are -- this effective tumor incidence numbers are lower over here for lung tumors compared to the metal study. That's probably because -- I didn't check, but it's probably because for cobalt sulfate, the tumors were showing up later than they did for cobalt metal. So more animals are dying due to other causes before the appearance of this first -- before a first appearance of this tumor.

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DR. DODGE: Okay. We also had to calculate the daily dose. And this is just a table showing our daily dose in milligrams per kilogram day. And again, that was

using the equation up there at the top, the inhalation rate times concentration over body weight converting that -- you know, the chamber concentrations to a daily dose.

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DR. DODGE: And then we plug it into the Benchmark Dose Software. And in this particular example, this is also in male rats, as we showed for cobalt metal, the lung tumors in male mice. I'm sorry. It's lung tumors in male mice here. So the benchmark dose and BMD and BMDL are shown in the lower left. Those are the vertical black lines. And as you notice, it's situated closer to the lowest non-zero dose there.

So we didn't have the issues with the Benchmark Dose Software we did for cobalt metal or we're getting a questionable response when used a BMR of five percent.

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DR. DODGE: Going on to the next slide. Here, we look at the highest cancer slope factor we derived for -- in male rats, female rats, male mice, and female mice. As you might expect, the highest cancer slope factor -- human cancer slope factor we derived was when we combined the two different tumor types, we saw that increased in female rats. That was the adrenal medulla tumors and the lung tumors. And when we combined that, we have a cancer slope

factor of 13.41.

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DR. DODGE: Now, because this was in cobalt sulfate heptahydrate, we need to normalize to the cobalt content in the sulfate heptahydrate. This is because the cobalt ion is considered to be the primary factor for cancer risk. So the cobalt sulfate heptahydrate cancer slope factor was normalized to the content of cobalt from the specific NTP study.

Now, there was another hitch here. Even though NTP throughout their entire document talks about cobalt sulfate heptahydrate, what they actually found they exposed their animals to was the hexahydrate, which I show in red there. It was 6H2Os rather than seven.

Now, the heptahydrate dehydrates to the hexahydrate at a temperature of 41.5 degrees centigrade, which I think is equivalent to about 107 degrees Fahrenheit. The NTP, even though they talk about heptahydrate throughout their document, and in nature you would be exposed to the -- most likely exposed to heptahydrate, their particular particle generating system resulted in the animals being exposed to the hexahydrate. They only mentioned this in a few sec -- a few paragraphs in their document.

And this was pointed out in our -- in the

comments that we had used the heptahydrate rather than the hexahydrate to normalize the cobalt contents anyway. The point is here we use the hexahydrate, the same form of the sulfate -- the cobalt sulfate that the animals were exposed to in order to come up with a cancer slope factor, and that was 3.0 milligrams cobalt per kilogram day to the minus one.

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DR. DODGE: Now, the last calculation we need to do - we're almost done here - is what's called an inhalation unit risk. This is simply taking the cancer slope factor and converting it to a form -- or to units of micrograms per cubic meter to the minus one. So this equation is the IUR is equal to the cancer slope factor times the breathing rate over the body weight times the conversion factor.

So the human breathing rate we use is 20 cubic meters per day. Average body weight is 70 kilograms. And the conversion factor is 1,000. This results in a cobalt metal IUR of 7.8 times ten to the minus three micrograms per cubic meter to the minus one. For cobalt sulfate, that IUR is about ten-fold lower, 8.0 times ten to the minus four.

So what do these numbers mean? Well, for the metal, lifetime exposure to one microgram per cubic meter

results in 7.8 chances of cancer in 1,000 individuals exposed. This is equivalent to 7,800 chances of cancer in a million individuals exposed.

For cobalt sulfate, heptahydrate, lifetime exposure to one microgram per cubic meter results in 800 chances of cancer per million individuals exposed.

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DR. DODGE: Would we like to entertain any more questions or should we go on to response -- comments and responses.

CHAIRPERSON ANASTASIO: Yes. But first, are they any questions specifically on the presentation?

Any other?

Ahmad.

PANEL MEMBER BESARATINIA: Very nice presentation. I just wanted to --

THE COURT REPORTER: Get closer to the mic.

PANEL MEMBER BESARATINIA: Oh. Yeah, I just wanted to go over the cancer slope factor derivation slide number 30.

CHAIRPERSON ANASTASIO: Was that 30 or 13?

PANEL MEMBER BESARATINIA: 30, 3-0

DR. DODGE: 3-0?

PANEL MEMBER BESARATINIA: Yeah.

DR. DODGE: Okay.

PANEL MEMBER BESARATINIA: So it's slide number 30, page 16. Go back one slide.

CHAIRPERSON ANASTASIO: I think -- is this the slide you wanted?

PANEL MEMBER BESARATINIA: Oh, yeah, this is the one. Yeah. Here, you have introduced this formula to account for interspecies differences. And you are indicating the body weight scaling, which can basically take into account the pharmacokinetic and pharmacodynamic differences within human and rodents.

What I'm wondering is, not specific to cobalt, but in general, for all inhalatory carcinogens, clearly, there is a great deal of difference between the anatomy of a respiratory tract in rodents versus humans. The nasal cavity in mouse and rats is highly complex and enables them to filter out the vast majority of the inhaled particles, whereas, humans is much simpler. And I'm wondering is it accounted for anyway in this calculation, is anatomical differences?

Because clearly, the dose -- the effective dose is not the dose to which the animal is exposed. The deposition of particle is far lower than the amount of the cobalt that these animals are being exposed to.

DR. BUDROE: Yeah, this is similar Dr. Kleinman's earlier comment. And right now, we don't have -- you

know, eventually, we might be able to work in something like the NPPD model and account for deposition, but right now we're just not at the technical point of being able to implement that. And, you know, even, for example, U.S. EPA isn't doing that right now either.

So it's something that we might try to do in the future, but we're not there yet. And this -- the interspecies scaling factor doesn't really account for that. It's more for peak PBE and, you, know pharmacokinetic pharmacodynamic differences. It's not so much for deposited dose. You know, taking and exposed dose to an absorbed dose.

PANEL MEMBER GLANTZ: Is there -- is there any data -- you know, leaving aside doing fancy modeling, but is there any data of like what fraction of the exposed dose actually gets absorbed for cobalt? Does anybody know?

DR. BUDROE: No, there's no empirical data out there for that.

PANEL MEMBER BESARATINIA: One thing we have observed from our own study is that we have to increase the amount of dose 100 times, sometimes even 1,000 times, in mice in order to produce the effects that are present in humans when they're exposed to, let's say, one-hundredths of the dose or one-thousandths of the dose.

So there is a clear difference between the dose -- effective dose between humans and rodents.

DR. BUDROE: ANd would you be talking about -- is that PM, for example?

PANEL MEMBER BESARATINIA: It could be. It could be, for example, particulate matter as a index for that.

DR. BUDROE: Yeah, there's some things like my kind of seat-of-the-pants perception of the -- comparing sensitivity of rodents to humans. Like humans seems to be a lot more sensitive, for example, to diesel exhaust than rodents. You know, you see a cancerous -- a cancer response in humans that's much greater for the same concentration than you would see in rats and mice or some things where it's -- the reverse is true.

So it's probably going to go on a chemical-by-chemical basis. And we're -- don't have any empirical data for cobalt where we can really tease that out.

PANEL MEMBER BESARATINIA: Okay.

PANEL MEMBER HAMMOND: In terms of the deposition, that's going to depend on particle size, of course. And I don't -- I was going back. You were saying that they called it heptahydrate, but it was actually hexahydrate. And I didn't read the original paper, so I apologize for that. But how -- how were they actually

producing the material they were exposing the animals to? Was it -- was it at the higher temperatures that they were producing it? And do -- do they -- you know, to say which is the right way to calculate, that really would depend on whether they were weighing it before and it got converted in the air, so it's a different thing, but you wouldn't take that into account in the calculations. It just depends on when the weighing was done.

DR. BUDROE: Well, I believe it was partly the way that they were actually generating the aerosol and it was heating the material up enough that it essentially desiccated it. You know, you drop that one water molecule.

PANEL MEMBER HAMMOND: But I guess if they weighed the material before they heated it up - that's the weight that they're thinking the dose is - then you actually still want to say heptane in terms of calculating the cobalt equivalent value, because that's from which it was weighed. And --

DR. DODGE: Well, they were -- they had -- they used methods to actually measure what the animals were exposed to in the chamber.

PANEL MEMBER HAMMOND: Okay.

DR. DODGE: And they -- yeah, in the pro -- you know, they started with cobalt sulfate hexahydrate in

solution and then atomize it, you know, blowing it out into the chamber. They didn't describe heating it, but it's certainly possible they do in the process.

PANEL MEMBER HAMMOND: Oh, so, if -- were -- they actually were having it aerosolized in a solution, so it --

DR. DODGE: From a solution, yeah.

PANEL MEMBER HAMMOND: Right. So we're not talking about the --

DR. DODGE: It desiccated.

PANEL MEMBER HAMMOND: -- cobalt sulfate particles. We're talking about a solution that has -- a water droplet that has that in it too. So therefore, the particle -- the particle size might be known if the aerosolization of the nebulizer was known.

DR. DODGE: The particle size is between one and three microns. That's what they -- they described it.

CHAIRPERSON ANASTASIO: All right. Thank you. Let's take a break, five-minute break. So we'll reassemble at 11:10. And then we'll go through the comments relative quickly.

(Off record: 11:05 a.m.)

(Thereupon a recess was taken.)

(On record: 11:15 a.m.)

CHAIRPERSON ANASTASIO: Let's get started again.

Take it away, Daryn.

DR. DODGE: Okay.

--o0o--

DR. DODGE: Comments and responses. We got comments from ToxStrategies, Cobalt Institute, and the Cobalt Pigments -- I'm sorry the Color Pigments Manufacturers Association.

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DR. DODGE: These are just going to be the main comments. There were a couple -- some minor comments that I didn't include in the slides here. But they were all in the -- our responses were to everything, to every comment. And you'll -- you got that in the package that we sent out a month ago. So I'm only covering the main ones here.

Okay. So I'll go on to the first comment.

ToxStrategies asked to clarify that cobalt alloys, in addition to cobalt-tungsten hard metals should be excluded from the cobalt and cobalt compounds categories, in other words not included in the cancer slope factors that we developed for cobalt compounds.

And we -- OEHHA agrees that cobalt alloys should not be included in the cobalt cancer slope factor categories. And we do say this in the document that cobalt alloys have different chemical and physical properties compared to the cobalt compounds in the NTP

studies in particular.

Some alloys are quite carcinogenic, For example, cobalt-tungsten hard metals. And they would require a different cancer potency factor than the ones we developed specifically for the cobalt compounds in metal.

Other alloys -- cobalt alloys are insoluble in weak acids and likely present no cancer risk. So again, we did not include cobalt alloys, you know, with the cancer slope factors we developed.

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DR. DODGE: Comment number two. Water solubility is a poor surrogate for solubility of metals under physiological conditions. But we had three parts -- or divided into three parts our response here.

Number one, solubility appears to play a role in cobalt-induced lung cell genotoxicity and suggests soluble and insoluble forms of cobalt. And they have different cancer -- or carcinogenicity potentials. As I mentioned earlier, the insoluble forms, such as cobalt metal, appear to be quite more potent in producing cancer compared to the soluble forms of cobalt salt -- cobalt compounds.

Point two here is categorization based on water solubility works well under insoluble -- because insoluble cobalt metal and compounds appear to be largely internalized by cells as particles.

And point three, keeping the classification information simple based on water solubility, whether it's greater than or less than 100 milligrams per liter, is adequate in determining which cobalt IUR, or cancer slope factor, to use.

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DR. DODGE: Next slide, comment number three. Comparison of cobalt sulfate, heptahydrate cancer potency to that of cobalt metal should be based on one content of cobalt and cobalt sulfate heptahydrate, not the content of cobalt sulfate. And point two here was NTP actually found rodents were exposed to the hexahydrate not the heptahydrate form of cobalt sulfate.

So regarding the first point, we corrected the comparison of cobalt metal based on the content of cobalt, cobalt sulfate heptahydrate. They're specifically referring to a paragraph or two that I wrote in the cancer hazard evaluation section, section four, where I made a comparison between cobalt metal and cobalt sulfate. And it actually should have been specifically to the cobalt content in cobalt sulfate. So I corrected that.

In part two, already explained the problem with the NTP study. They actually exposed the animals to the hexahydrate. And this comment in particular, you know, alerted to that -- alerted us to that. We hadn't caught

that, because it was only mentioned in a paragraph or two in the NTP document.

But this only adjusted the cancer slope factor slightly. It went from 2.8 to 3.0 milligrams per kilogram day to the minus one.

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DR. DODGE: Comment number four, this comment is mainly by ToxStrategies here. Suh et al. converted the two forms of cobalt to human equivalent concentrations using the EPA RDDR method, which is regionally deposited dose ratio and found the carcinogenicity or potency to be similar.

Now, this is a graph from Suh et al. And what ToxStrategies in particular is suggesting is that if you connect the two blue lines, you could form a single line through all of those blue points resulting in one cancer slope factor that would -- can be used for both cobalt sulfate heptahydrate and cobalt metal.

Likewise, you could combine the two black lines there and come up with one slope. They didn't actually plug this information into the U.S. EPA Benchmark Dose Software. They're just saying it looks like it's -- you could make one line out of the combined metal and sulfate data. The cobalt metal data is the -- is up in the upper right. And the cobalt sulfate heptahydrate data is in the

lower left-hand side.

It's -- you know, it looks like it's possible, but we have to consider the fact that the metal is more -- is likely more potent carcinogen than the cobalt sulfate heptahydrate. So if you draw a line specifically through the data in the top right-hand corner there, the mouse and rat data, you would get a steeper slope than drawing a line through just simply the hexahydrate data in the lower left.

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DR. DODGE: And that's what I -- that was our response here is that we're going to be health protective and assume just like what the genotoxicity and lung cell culture data tells us that there is definitely a higher potential for cobalt metal to be more toxic, more potent in terms of carcinogenicity compared to the soluble cobalt compounds. So we would prefer to do slope factors individually for cobalt sulfate heptahydrate and cobalt metal.

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DR. DODGE: Comment number five, OEHHA did not use dosimetric adjustments appropriate for each tumor site, which is inconsistent with U.S. EPA guidance and ignores the importance of variable lung deposition by particle size and species.

Our response is that because there is evidence of systemic distribution of inhaled cobalt resulting in systemic tumors, we used body weight scaling to convert to human equivalence. This is a method used by OEHHA for extrapolating from rodents to humans for cancer potency derivations. Using this interspecies scaling factor is preferred by OEHHA, because it assumes -- assumed to account for not only pharmacokinetic differences but pharmacodynamic considerations as well.

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DR. DODGE: And comment number six, the latest version of BMDS, or Benchmark Dose Software, 3.1 now contains recommendations and warnings for model selection of the BMR. A BMR of five percent for lung tumors in male mice resulted in a questionable recommendation, because the five percent response rate is not within the observable range.

Now, we did go over this earlier. But they went on to comment that the custom BNR -- BMR method is recommended, which has been used previously by U.S. EPA in 2011. In U.S. EPA's method the custom BMR is calculated as follows. And this is the equation they use to come up with a different benchmark, or BMR value, to use.

This particular method when applied to the mouse data resulted in BMR of 78 percent, which they say is

within the observable range.

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DR. DODGE: Our response is that, as noted earlier, OEHHA recommends using the exact formula when the BMR five percent yields a BMD that is not within the observable range. The U.S. EPA BMD version 3.1 software shows that a BMR of 15 percent gives a "viable" recommendation in the middle. And applying the exact formula results in a CSF of 4.57 is -- and is the same regardless of whether the BMR is five percent or 15 percent.

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DR. DODGE: Now, to go on with the comment number six here. In this graph, we show what a -- using a BMR of 15 percent looks like. A BMR of five percent would be a little bit lower on the line, a little bit closer to that control group there in the bottom left. But you get up to 15 percent, and now you get what's called a "viable" recommendation rather then a "questionable" recommendation.

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DR. DODGE: Okay. And so ToxStrategies, in their Suh et al. paper, recommended, you know, using this so-called BMR custom method, which came out of a EPA document. Using a BMR of 78 percent, which is -- comes

out of this so-called custom method equation, it shows a BMD and BMDL that is in between the low- and mid-dose group. And we really don't think that's health protective. We're really interested in what's going on between the control and the low-dose group.

So we don't think this method is appropriate. In addition, the custom BMR method, as suggested by ToxStrategies, came out of a 2011 document, as I noted earlier. But this was actually an external review draft document that had never been finalized.

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DR. DODGE: Comment number seven, OEHHA modeled pheochromocytomas in rats both independently and as part of a combined analysis. There is evidence that pheochromocytomas arise in inhalation studies where hypoxia is induced as a consequence of exposure to particulate producing lung lesions, including tumors.

Thus, it is unnecessary for pheochromocytomas to serve as the basis of any cancer slope factor or IUR alone or in combination when a more relevant cite of contact tumor is present.

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DR. DODGE: Our response was in two parts here. Due to the lack of competence by NTP and other researchers have for the cause of rat pheochromocytomas, OEHHA has

chosen a health protective approach by assuming that pheochromocytomas arise independently from the lung cancer and non-cancer effects.

And point two, a number of NTP carcinogenicity studies observed pheochromocytomas resulting from a carcinogenic chemical that was put in feed or administered by gavage. And there was no pulmonary effects found in these studies. Therefore, OEHHA cannot ignore the possibility that inhaled cobalt metal and cobalt compounds that are absorbed systemically and reach the adrenal glands could be a direct cause of pheochromocytoma.

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DR. DODGE: Comment number eight. Due to increasing morbidity of the F344/NTac rat colony and the lack of historical control data, the occurrence of systemic tumors in the cobalt metal study in rats cannot be conclusively interpreted. In other words, they wanted this particular rat data thrown out.

We responded by saying NTP did not express concern that the strain of rat used in the cobalt metal study would affect the carcinogenicity incidence. Some non-cancer endpoints may be affected, but not the cancer endpoints.

And point two here is that OEHHA ultimately derived a cancer potency factor for cobalt metal based on

the lung tumor data in male mice. So we didn't even use this particular rat data.

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DR. DODGE: In comment number nine, by the Cobalt Institute, the combination of both cobalt compounds into one dose response curve results in a very good model fit. The indication that the model is able to predict exposure responses at relatively low exposures. A detailed report on benchmark dose modeling of the complete animal data set is appended to these comments.

So what Cobalt Institute did is they actually ran a dose response, or benchmark dose modeling, using the combined cobalt metal and cobalt sulfate data and came up with one -- well, one dose response curve for both the metal and the sulfate. Hence, it resulted in one cancer slope factor for both of these compounds combined.

The resulting BMDL value was 0.12. And so we did -- we calculated the cancer slope factor or -- from that. And that was a rodent cancer slope factor of 0.42 from their data. They chose a 90 percent confidence interval bound around the BMD. Typically, we would use a 95 percent confidence interval around the BMD. So that 0.42 cancer slope factor should be actually a little bit higher by our methodology.

But in any case, compared to the cancer slope

factors we came up separately for the metal and the sulfate, that number they that the Cobalt Institute came up with using Benchmark Dose Software isn't that much different than our cancer slope factor we came up for the sulfate which was 0.74 milligrams per kilogram day to the minus one.

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DR. DODGE: For cobalt metal, the slope factor was actually -- was quite a bit higher, 4.57. Again, as outlined earlier -- in our earlier response, the lung tumor incidence slopes for cobalt metal appear to be steeper than the lung tumor incidence slopes for cobalt sulfate heptahydrate in both rats and mice. And we chose to calculate cancer slope factors separately for the two forms for cobalt.

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DR. DODGE: Comment number ten. Cobalt compounds such as cobalt oxide and cobalt sulfide have negligible solubility of around one to two percent in biological fluids, namely artificial alveolar or lysosomal lung fluids. And they should not be grouped with cobalt metal powder for endpoint inhalation toxicity. So they would like these low solubility compounds thrown out and not included in the cancer slope factors.

And our response is in two parts here. In lung

cell cultures, you can see up to 50 percent solubility of cobalt oxide particles within cells. So using artificial alveolar or lysosomal lung fluids may not mimic what's going on in the cells very well.

In addition, a number of in vitro studies in the lung cells observe genotoxicity and cytotoxicity resulting from cobalt oxide exposure. Therefore, cobalt compounds of low solubility are grouped with cobalt metal.

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DR. DODGE: The final comment here that I have by the Color Pigments Manufacturers Association, it is inappropriate for OEHHA to categorize all compounds with solubilities lower than 100 milligrams per liter as essentially the same for inhalation risk assessment. Complex inorganic color pigments, particularly cobalt aluminum chrome spinel do not yield significant amounts of bioavailable cobalts. They would like to have this particular compound thrown out or not included in the cancer slope factors we developed.

Our response is that OEHHA agrees with that cobalt spinels should not be included in the cobalt cancer potency factors. And we now say this in the document. And the reason why is that calcining process at high temperatures used to form these spinels, it's an interdiffused crystalline matrix structure, which -- and

the process has similarity -- similarities to the alloying process. So as I noted earlier, we do not include cobalt alloys in these -- with these particular cancer slope factors that we developed.

In addition, spinels have very low solubility, even in lysosomal fluids. So we're talking about pretty low levels of 0.089 percent.

And the final point here is that IARC concluded there is currently inadequate evidence for carcinogenicity of cobalt aluminum chromium spinels. We do not include the spinels in our cancer slope factors.

All right. That's the end.

CHAIRPERSON ANASTASIO: Great. Thank you very much, Daryn.

So what I'd like to do now is start with our leads. I know we've already had quite and extensive discussion, which is great. We would like try to finish by noon, so let's try not to repeat ourselves from the earlier discussion. But if we have items that are new, let's talk about those.

Ahmad, would you like to start? Anything to add?

PANEL MEMBER BESARATINIA: Well, one thing I just wanted to mention is that perhaps it was not covered in this part of your presentation. It was regarding the way that the genotoxicity mutagenicity of cobalt was presented

in this draft. And it appeared to me that it's not very balanced considering the existing data that shows lack of mutagenicity and genotoxicity of cobalt in mammalian cells, as well bacterial systems.

And it's just -- sitting outside and looking in, it appeared to me as if it is kind of going out of its way to show the positive data. So perhaps a more balanced presentation of the current data that are available in the literature help to make it a fairer review.

DR. DODGE: I can -- yeah, I could do that. I concentrated on the data that NTP generated in terms of the Ames assay results. I figured that was the best data that we had available for that type of assay.

Yeah, and I -- I only -- I only referred to -- you know, that there were other studies that were done in the past, but I could, you know, add a few more of the more recent ones.

PANEL MEMBER BESARATINIA: There is no question that the carcinogenicity is out of the question. But you don't need to demonstrate that it's mutagenic in order to be carcinogenic, because more and more papers are coming out showing a nongenotoxic mode of action for this chemical, particularly the pathways involving alloys and oxidative DNA damage. And even more recent papers show an epigenetic mechanism involved. So perhaps that would help

the argument.

DR. DODGE: Okay.

CHAIRPERSON ANASTASIO: Thank you, Ahmad.

Joe.

PANEL MEMBER LANDOLPH: Yeah, I appreciate all the effort you, John and -- you put into the document. It's very well written, well organized. I'm just going to skip over some of my comments.

And I like the nice concise summary of the animal carcinogenicity bioassays. That was great data. And I think you're absolutely right the differentiation between the metal and the insoluble compounds versus the soluble ones. I agree with you completely and I don't agree with the reviewers that made the other comments, because that's exactly the way nickel goes and chromium as well. There's a big difference between the insolubles being phagocytosed and having a greater carcinogenic effect compared to the solubles. And with nickel -- soluble nickel, it just doesn't work in animals. It comes out in urine, because there's not biological receptor.

A little bit of soluble nickel gets in on the iron transport carrier, but it's not enough to cause carcinogenesis. So I think on your responses to number two, and number four, and number 11, you're right on the money. I would not budge on that. I think you're

Absolutely right.

Let's see, what else?

And I feel the pheochromocytoma data is a little shaky. I think I'd stick with the lung alveolar benign and malignant tumors. I think you're much better off.

The epidemiology you've gathered together. It doesn't show very much. I think that's the way it is and that's the way it will stay for quite awhile.

And your discussion of the genotoxicity was very interesting, I thought, that you get comet assay increases this the percentage of the tail, so that -- that was pretty clear some type of damage was going on in the oxygen radical damage and that you -- it altered base DNA products, which were typical of hydroxyl radical attack. That's very interesting and I think that's probably important in the mechanism.

I agree with Ahmad for arsenic, nickel, and chromium, Max Costa's lab has shown that in addition to all the genotoxicity studies done, they're getting epigenetic effects, changes in methylation histones and how that affects gene expression also. Many of these metals seem to have a bifurcated type of mechanism, two mechanisms going on at the same time. So it's a complicated mechanism, I'm sure.

But I think it's an excellent document based on a

thorough analysis of the carcinogenicity and genotoxicity of cobalt metal and insoluble cobalt salts, and on the carcinogenicity of the water soluble cobalt compounds normalize the cobalt content.

So I thought the document was pretty good. And you have the other comments we made with regard to the slopes of the curves and all of that stuff. From the transcript, you can get our comments from there.

I liked using a linearly fit models and comparing it to the other one, something like that. I think the document is terrific. It's very strong.

CHAIRPERSON ANASTASIO: Thank you, Joe.

I'd like to open it up to other Panel members. Any additional comments?

PANEL MEMBER KLEINMAN: This is Mike.

Just following up on Dr. Hammond's comment earlier, you don't -- you didn't have any hot spot actual environmental measurements. Are there, you know, any data that could be added to the report to give us an idea of what the actual exposures are cobalt?

CHAIRPERSON ANASTASIO: Near hot spots?

PANEL MEMBER KLEINMAN: Yeah.

DR. BUDROE: We didn't find any. You know, if it had been out there, we would have included it in the document. So, I mean, we put everything in that we could

find.

PANEL MEMBER HAMMOND: Do we know what are the hot spots in California for cobalt?

DR. BUDROE: Aerospace metal finishers, cement kilns, some other combustion -- some other facilities that use extensive material combustion. But I would say that the two top of the list would be aerospace metal finishers and cement kilns.

PANEL MEMBER HAMMOND: I would have thought there might have been some sampling near cement kilns conducted. I don't know that. I just --

DR. BUDROE: Well, it's the chicken and the egg problem. They -- if they did sampling, they probably didn't do -- include cobalt in the list of analytes because it's not a problem.

CHAIRPERSON ANASTASIO: Other Panel comments?

PANEL MEMBER KLEINMAN: Well, I guess the other piece of data that you do have though are the emissions inventories, right, where you could at least identify areas where there might be exposures.

DR. DODGE: Well, all we had was the regional sort of exposures over urban areas, where it was clearly higher -- you know, considerably higher when you compare it to the rural or wilderness areas. That's the best we could find.

CHAIRPERSON ANASTASIO: I mean, even in the absence of hot spot measurements, those upper bounds that you gave for some of the urban areas in Southern California are above one in a million risk, based on your IUR.

DR. DODGE: Yeah, that was noted by one of the commenters.

CHAIRPERSON ANASTASIO: Yeah. So clearly, you know, near a hot spot, you're going to have an issue.

PANEL MEMBER RITZ: Yeah. I would actually recommend that you describe a little bit what you just said in the introduction where the hot spots could be from industry. And TRI data does not report cobalt, because it's not a problem?

DR. BUDROE: Well, TRI data does report it, but they -- you can't get it -- like a hot spot concentration estimation out of it.

PANEL MEMBER RITZ: Yeah. No, that's not what I meant. What I meant is maybe you can describe the TRI facilities that are reporting on cobalt so you have an idea of what industries those are.

DR. BUDROE: Right. Well, we can do that with the ARB -- with the hot spots inventory data. So we could make a mention of, you know, what types of facilities are likely to produce cobalt emissions in California. And

maybe an estimation -- like a range of magnitude of how much they're putting out. So we could do that. We could add that to the document.

PANEL MEMBER RITZ: That would be very helpful. Thanks.

PANEL MEMBER LANDOLPH: Yeah, I would agree with that, because I was looking at your slide two quite a while ago. And, you know, from the wilderness and rural areas up to the high amounts of mean air concentrations in the urban areas, that's 1,000- to 10,000-fold increase. I mean, that's huge. That's enormous. I would certainly agree with the other two reviewers to discuss it a little bit.

DR. DODGE: Yeah. Those -- those higher concentrations you see in urban areas. It's largely from various combustion sources as you might expect.

PANEL MEMBER BLANC: Well, why would I expect that there would be cobalt from combustion?

DR. DODGE: Just that -- you know, there's various -- you know, some very small amounts, but there are metals, for example, in diesel fuel. And you combust diesel, it's going to release these metals. I mean, if there's any coal sources, combustion in coal, you're going to get metals put in in the air.

PANEL MEMBER BLANC: Oh, so you're -- so you're

saying that the predominant source of diffuse ambient air pollution cobalt is likely to be fossil fuel used?

DR. DODGE: Various fossil fuels. Yeah, some more than others. I -- you know, if you'd like, I could probably go into that a little bit --

PANEL MEMBER BLANC: I mean, it's not in there --

DR. DODGE: -- as to why it's higher urban areas?

PANEL MEMBER BLANC: It's not in there now, particularly or it's --

DR. DODGE: I'm sorry?

PANEL MEMBER BLANC: It's fairly obscure in the document that a substantive proportion of ambient low-level pollution as opposed to high-spot pollution is likely to be from fossil fuel combustion as an actual contaminant of fossil, if that's what you're saying?

DR. BUDROE: Well, it's -- that gets to be a little harder to make that exact connection, because, for example, cement kilns, we can't really say if -- for sure nobody has actually done a study that we're aware of to check to see is it the materials going into the cement kiln, is it the combustion process itself?

We just know that cement kilns, you know, are one of the leading emitters of cobalt. You know, exactly what the pathway is for that happening, you know, we don't have that information. There's other things like, for example,

motor vehicle traffic. There's a certain amount of cobalt gets used in things like pistons, and piston rings, and such that could be a contributor. But we're hypothesizing. We don't have, like I say, a U.S. EPA document that's looked into this and says, yes, this is where -- you know, if you have urban air and you've got this much cobalt, where is it coming from? So we're kind of making educated hypotheses.

CHAIRPERSON ANASTASIO: Other comments?

Lisa.

PANEL MEMBER MILLER: Yeah I just had a quick comment.

When I went through the document, and I may have missed this, there wasn't much of a discussion on susceptible populations of kids, right? And I realize you're limited in terms of the data that you can draw from. Was there -- was there any consideration of, for example, in your calculations, of an increased respiratory rate in children and how that might, in fact -- it just -- it goes back to potentially underestimating those.

DR. BUDROE: Well, that would -- we don't so much consider that in the actual document that does the hazard identification and the dose response analysis. But once we develop a cancer unit risk, that will go into the hot spots facility risk assessment software where we did --

you know, the Panel approved the guidance manual back in 2015, and that includes both tailored breathing rates by age group and also the use of the age-specific factor. So infants and children are expected to have a higher cancer risk if they're exposed at young ages than adults.

So that's taken in consideration, but at a later part of the risk assessment process.

PANEL MEMBER MILLER: Okay. Thank you.

CHAIRPERSON ANASTASIO: So I have a somewhat related question. You know, if you take the unit risk factor and convert it to an equivalent concentration that would result in a one in a million risk, you get about 0.1 nanograms per cubic meter for cobalt metal and about one nanogram per cubic meter for soluble cobalt.

So then the mean Southern California concentrations are above that. So it seems that entire Southern California is a hot spot for cobalt. And so what do you do in that case? If most of your population is being exposed at a level -- I mean, is one in a million the level at which you start to worry about the risk or am I not correct on that?

DR. BUDROE: Well, for example, South Coast AQMD has -- requires risk notification at ten in a million. So -- and I think risk reduction at 25 in a million.

CHAIRPERSON ANASTASIO: Risk reduction at 25 in a

million. Okay. So you're getting -- some of these are going to be close to that, if it's cobalt metal.

DR. BUDROE: That's a -- I mean, it would -- it would depend on where it was. If you had a cement kiln out in Victorville and there's -- you know, out in the middle of nowhere and there's nobody out there, it might not. But if they were in say City of Industry with the residential population, then yeah. You know, it's going to be on a site-by-site basis.

CHAIRPERSON ANASTASIO: Right. No. What I'm saying is that these mean air concentrations in urban Southern California, it's close. You know, 25 in a million would be 2.5 nanograms per cubic meter of cobalt metal. So certainly some of these maximum levels, you're going to -- it seems like you're going to have a lot of hot spots, which would be interesting and hopefully something we can do something about.

DR. BUDROE: Correct. Well, this will be -- this will -- it will be interesting to see downstream as this number gets adopted as to what effect it's going to have on hot spots facility risk assessments.

CHAIRPERSON ANASTASIO: I have one other comment. It was about the cobalt-tungsten carbide which appears to be more carcinogenic. Is that something that is common in California that we should be expecting emissions on that?

PANEL MEMBER BLANC: Yes, it's very common in California.

CHAIRPERSON ANASTASIO: Oh, it is very common in California.

PANEL MEMBER BLANC: It's ubiquitous, I would say, in terms of any place where there's a hard metal cutting blade used. That would include anywhere that has industrial level saw blades or dental labs that have tungsten-cobalt drills, or any other number of places, which would be the one area that I wanted to ask you to be a little bit more clear in the executive summary, which, in fact, does not distinctly mention hard metal. It refers to alloys.

In your presentation, you were clearer in your first slide, but in the executive summary not clear that that's being talked about. And since later suddenly in the document, at a certain point, it says not only this is more carcinogenic, but this was not covered in this document.

I think it -- you know, and that's worthy of being clarified in the executive summary, so that nobody will be surprised on that.

DR. DODGE: (Nods head.)

PANEL MEMBER BLANC: And because technically tungsten-carbide cobalt is not an alloy. In the

metallurgic sense, it's in this other category of pseudo-alloys or whatever. It's not a true alloy, unlike the steel cobalt alloys. So if you use the word alloy, it wouldn't subsume tungsten-carbide

DR. DODGE: No, I didn't realize that they called it a pseudo-alloy. I haven't seen that term.

PANEL MEMBER BLANC: Well, they don't call it. I'm using that generically. No, that's my made-up term.

DR. DODGE: Okay.

PANEL MEMBER BLANC: It's not an alloy at all. It's a something. They refer to it as a --

DR. DODGE: The process, as I understand it, they heat it just enough so that --

PANEL MEMBER BLANC: It sticks together.

DR. DODGE: -- the dust particles stick together, yeah. And when that happens, you get this different type of process here.

PANEL MEMBER BLANC: Right. Conglomerate. Right. I don't -- I actually have never been clear what the technical term -- I mean, it's often made through a centering process.

But anyway, that's too much detail, but it's not -- it's actually a mentioned in the executive summary, where alloys are mentioned, but not this.

DR. DODGE: Okay. I'll fix that.

PANEL MEMBER BLANC: And it should also say that there won't be included here --

DR. DODGE: Right.

PANEL MEMBER BLANC: -- even though it's more carcinogenic.

And I thought it was good that you at least alluded to the severe lung disease that -- that that substance causes. Actually, probably cobalt alone without that can probably cause giant cell pneumonitis as well. Again, I don't know if that's too much detail for you to go into, because those cases where that disease occurs with pure cobalt. You know, it's by far not as common.

DR. DODGE: I could mention that. I believe that type of lung disease by cobalt -- caused by cobalt alone is also considerably less than combined tungsten and cobalt.

PANEL MEMBER BLANC: Yeah, yeah. It's not as -- it's much rarer, but -- and a lot of -- even a lot of specialists don't realize, and think it can only be caused by tungsten cobalt-carbide. And cobalt also is one of the metals which potently con cause asthma. And since insensitized workers. Again, I'd -- it's at your discretion if you want to -- you have not talked much at all about the other serious health effects of cobalt. And I don't know if it's too much of a diversion to have one

or two sentences where you talk about it.

But, you know, cobalt is quite an interesting toxic metal. And it's -- you know, its association in metal-on-metal hip disintegration and severe cardiac disease, as well as deafness. So it's ototoxic. It's cardio toxic. It's an interesting substance. I don't know --

DR. DODGE: That's getting a little bit outside of what we're trying to do. You know, this is a cancer document and --

PANEL MEMBER BLANC: I understand that. But you do talk -- I think it is appropriate that you have --

DR. DODGE: Yeah.

PANEL MEMBER BLANC: -- a sentence or two that tungsten carbide causes this other disease.

DR. DODGE: Yeah, we can do that.

PANEL MEMBER BLANC: So if you wanted to say just cobalt has other non-carcinogenic serious human -- well known human toxicities with one reference, it wouldn't be a terrible thing to do, but it's completely your editorial discretion. If there's enough reviews, you could just cite one of the reviews or something.

DR. DODGE: Okay.

PANEL MEMBER BLANC: Okay. Because people who read the document who know cobalt, you know, will have

that in their mind, because this was such high profile stuff. And I grant you, it's not -- some of these effects are by systemic absorption and not at all through inhalation.

CHAIRPERSON ANASTASIO: Thank you, Paul.

Joe.

PANEL MEMBER LANDOLPH: Well, I was on the NTP panel that dealt with cobalt tungsten carbide and it's phagocytosed very well. And that undoubtedly contributes to its carcinogenicity, you know, as a mechanism of uptake. So it was notable how well it was phagocytosed and how carcinogenic it was.

CHAIRPERSON ANASTASIO: Is cobalt tungsten carbide on OEHHA's radar for a cancer potency factor?

DR. BUDROE: Not right now. I'm truthfully not up to speed on what the -- if -- for example, if there's any NTP study out there that we could use or not.

CHAIRPERSON ANASTASIO: Any other comments from the Panel?

Yes, Stan.

PANEL MEMBER GLANTZ: Well, just for the record, when I met with the OEHHA people yesterday, I found a few spots in the document that I thought weren't clear and we talked about how they could rewrite them to clarify some things. There are no substantive changes. I just

wanted -- and they've got that.

But -- so I'd like to come back to my suggestion that the alternative analysis with the slope -- you know, the 15 percent and all that be dropped. I think you can leave it in that the program said that there's concern about the extrapolation. But then you can say that the concern is that we're underestimating the risk.

But, I mean, the difference, as you pointed out, between the direct estimate and the alternative is trivial. And I think all you're doing is making it unnecessarily complicated. So I really think that ought to be deleted.

CHAIRPERSON ANASTASIO: So are you saying the alternative treatment with the quote/unquote exact calculation should be deleted?

PANEL MEMBER GLANTZ: No.

CHAIRPERSON ANASTASIO No.

PANEL MEMBER GLANTZ: It's not really an exact calculation.

CHAIRPERSON ANASTASIO: Right, that's why I put the quotes around it.

PANEL MEMBER GLANTZ: Yeah, that's what they called it, but it's not. Again, it relies on the beta one parameter estimate, which came out of the curve fitting program, so all of the problems we talked about are

embedded in that. So I just think it's cleaner and more defendable. And in the end, it doesn't make much difference to just use the BMDL 0.05 that comes out of the program and just say, you know, the program highlighted that there's a lot of uncertainty, because the lowest positive dose is pretty high, and the consensus is that the uncertainty that's introduced means that we're almost certainly underestimating the risk. And it might be a substantial underestimate, but we don't know by how much and just leave it at that.

I just think it would be a lot cleaner. And then you don't have to get into an argument about why did you pick 15 percent, for example? And the truth is, well, it made the computer program happy, which we've all been critical of. And so I really think that should just be take -- I mean, it's a -- it will -- it will -- it's always easy to hit the delete button, you know. We're not -- I'm not actually adding anything. So I -- is that -- are people okay with that?

CHAIRPERSON ANASTASIO: I think that's a reasonable approach.

DR. DODGE: So what Stan is asking is that essentially that we're going to take our animal cancer slope factor of 4.57 and adjust it down to five percent BMR, which only results in a reduction of -- from 4.57 to

4.46. And when we round it --

PANEL MEMBER GLANTZ: Yeah, or if you round it off, they're both about 4.5.

DR. DODGE: Right. When you round it to a -- like in the end, round it to just one or two significant factors or numbers.

PANEL MEMBER GLANTZ: Yeah, it's not going to --

DR. DODGE: It's going to be really hard to -- little or no difference.

PANEL MEMBER GLANTZ: Yeah, that's right, but you just avoid one thing for people to -- like me to criticize.

DR. BUDROE: That sounds entirely doable.

PANEL MEMBER GLANTZ: Okay. Well, then having said that, I'd like to move that we accept the report subject to the modifications the Panel suggested, and then say that OEHHA can just give it to the Chair to review. And then if the Chair thinks it's okay, then it's done. If there are issues that the Chair thinks need to come back to the Committee, then we can have another meeting on it.

But I think -- I didn't hear any hugely serious criticisms of the rest of it. I'd like to move that.

PANEL MEMBER KLEINMAN: I'll second that.

CHAIRPERSON ANASTASIO: Okay. All in favor?

(Ayes.)

CHAIRPERSON ANASTASIO: Do a raise of hands and then I'll verbally --

(Hands raised.)

CHAIRPERSON ANASTASIO: Okay. So it's unanimous in favor of the motion. So we will take care of it from here. Thank you everyone.

We're going to take a break for lunch now. Reid is going to bring in lunch. And Lisa has to go teach, so we've bid her adieu. And I'd like to thank OEHHA for a very nice document. And we will reassemble at 12:30.

(Off record: 12:06 p.m.)

(Thereupon a lunch break was taken.)

A F T E R N O O N S E S S I O N

(On record: 12:35 p.m.)

CHAIRPERSON ANASTASIO: All right, everyone, welcome back. So our second major agenda item today is review of the proposed changes to the chemical substances list in Appendix A of the AB 2588 Air Toxics Hot Spots Emissions Inventory Criteria and Guidelines Regulation.

Just a little background first. So under AB 2588, certain facilities are required to report their emissions of specified toxic chemicals. The implementing regulation, which is known as the Emission Inventory and Criteria Guidelines Regulation, was last updated in 2007. And the California Air Resources Board is considering amending the regulation.

So Dave Edwards, the Assistant Division Chief of the Air Resources Board's Air Quality Planning and Science Division is going to provide us with an overview of the regulation and a summary of the changes being considered for the chemical list.

So I turn it over to Dave.

(Thereupon an overhead presentation was presented as follows.)

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: All right. Great. Thanks, Cort, for the introduction.

All right. So for my presentation today, I'm going to start with a general overview of the AB 2588 Hot Spots Program that briefly goes over some of the key points that we presented to you at the June 28th meeting. We'll then move into the main topic for today's discussion, which is your review of the list of chemicals that we are proposing to add to appendix A of the emissions inventory criteria and guidelines document.

I'll then provide a brief synopsis of the substance selection process, go over a number of questions that we would like you to consider for re -- and then go over a number of questions we would like you to consider for your review.

Lastly, I'll walk you through a number -- sorry, through the proposed timeline, the opportunities for public comment on the proposed list of new substances, and the process we envision for documenting the results of your review.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: All right. So just to start with a little bit of background. As you may recall, on June 28th of this year, CARB staff made a presentation to you, in which we informed you about our plans to update the Emissions Inventory and Criteria Guidelines regulation.

In that presentation, we provided information about the revisions that we were considering as part of the regulatory update, and also discussed the statutory requirements that guide the compilation and updating of the Appendix A chemical list. We also made a request for your assistance in reviewing the list of proposed new substances.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Next, I'd like to go over some of the key points that we previously discussed with you concerning the Air Toxics Hot Spots Program.

As you may recall, the goals of the program are to collect air toxic pollutant emissions data and make it available to the public; identify facilities that may have localized impacts; assess the risks to public health and notify nearby residents about significant risks; and reduce these risks to levels that are health protective.

One of CARB's responsibilities under this program is to develop and maintain the Emission Inventory Criteria and Guidelines regulation that provides direction to facilities on how to compile and report their air toxics emission data. A key piece of these guidelines is Appendix A, which provides a list of chemical substances that may pose chronic or acute health threats when present

in air and which must be reported as part of a facility's emission inventory. Under the regulation, facilities are required to report their emissions on a four-year cycle.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: In Appendix A, the emissions inventory guidelines, chemicals are grouped into three tables. Appendix A-I lists substances for which emissions must be quantified in a facilities emission inventory. These are substances with the potential to present adverse impacts to public health due to their toxicity and potential to be emitted to the air from operations at California facilities.

Appendix A-II substances for which their production use or other presence muss be reported. These are substances with recognized health effects, but for which the usage and potential to be emitted to the air in California are less certain. Information on the production and use of these substances helps CARB and OEHHA staff better characterize their potential to become an air pollutant that could create exposure to the public.

Then lastly, Appendix A-III lists substances that are required to be reported only if they are being manufactured in California by a facility subject to the program. An example of the substance that may be assigned to this table could be an oral pharmaceutical that would

not be expected to have airborne emissions of concern at its point of use, but for which the manufacturing facility could have the potential to release the material during manufacturing and handling processes.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: For this next part of the presentation, we'll present an overview of the selection process for the new substances, go over the documents that we did provide for your review, and also walk you through the questions we would like you to consider in your review.

So in the June 28th presentation, we briefed you about the six source lists of chemicals that CARB staff must consult for compiling an update in Appendix A of the chemical list. These lists include: California's Toxic Air Contaminant List; U.S. EPA's Hazardous Air Pollutants List; the International Agency for Research on Cancer; California's Prop 65 list; the list of the National Toxicology Program, which is an interagency program within the U.S. Department of Health and Human Services; the list of California Department of Public Health's Hazard Evaluation System and Information Service.

And also, the 2588 statute gives CARB specific authority to include additional chemicals that may present a chronic or acute threat to the public, but have not been

formally listed in the six sources mentioned earlier.

CARB staff, working closely with OEHHA and DPR, evaluated over 1,300 new substances using the following selection criteria:

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: First, the recognized toxicity under one of the six mandated lists or under CARB's authority; and the substance can become airborne and be present in California.

Our review resulted in 812 new substances being proposed for addition to Appendix A, with 639 substances being proposed for A-I, 11 for A-II, and 162 for A-III.

Also, through this process, staff did identify 548 substances that were deemed as not meeting the selection criteria due to insufficient evidence for cancer or non-cancer health effects or not being likely to become airborne.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: After the June meeting, CARB providing four documents to facilitate your view of the propose -- your review of the proposed new substances. The first was a document intended to provide the necessary background and context to understand the organization of the tables and selection criteria for the proposed new chemical substances.

The second document was a copy of the existing Appendix A list, which was intended to provide a reference of the types of substances already regulated under the program. This list contains substances in Appendices A-I to A-III of the current regulation, which was last fully revised in 1996 and only partly updated in 2007.

The third document, which was provided in both Excel and PDF formats, was the mater list of new proposed substances.

The last document consisted of several subsets of the master list grouped into eight different categories, requested in our June meeting. The categories are carcinogens, developmental and reproductive toxicants, pesticides, metals, other organics, pharmaceuticals, neurotoxins, and other. The other category --

PANEL MEMBER GLANTZ: Can I ask a question?

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yes. I was just --

(Laughter.)

PANEL MEMBER GLANTZ: Well, so why -- and why don't you -- I missed the earlier meeting. But why don't you have pulmonary toxicants and cardiovascular toxicants on the list?

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yeah. That is something additional we can consider. It's likely

in the other category at this point.

PANEL MEMBER HAMMOND: This is Kathy. Actually, when I looked at -- since he brought that up, when I was looking through the material, I found this way of laying it out confusing, because part -- partially it's outcomes and partially it's chemical categories. So it's kind of a funny mix, frankly, if you follow me.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yeah. And there is some overlap between the lists, so --

PANEL MEMBER HAMMOND: Right. Well, yeah, so I would think there would have to be.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yes.

PANEL MEMBER HAMMOND: So in other words, going to Stan's comment, we would -- there are a lot more outcomes we care about than just those.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yes. Yeah, and that's definitely understood. The list is pretty expansive, so, yeah, there's -- there's a lot of ways to slice and dice it.

All right. So to continue. The "Other" Category, which is the roughly 300 or so chemicals does have other categories within it, such as endocrine disruptors; respiratory, eye, or skin irritants; sensitizing agents and asthma triggers; persistent and bioaccumulative toxics; and, also chemicals that are being

proposed as part of new or already existing chemical groups such as isocyanates, polycyclic -- or polycyclic aromatic hydrocarbons, and PAH derivatives.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: So to kind of further go into the list a little bit of how the magnitude of these substances are broken down by the categories, as I just mentioned, you could see sort of the breakout on the slide above. As I mentioned earlier, note that some of these categories may overlap. So, for example, a substance could be categorized as both a pesticide and a developmental and reproductive toxicant.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: All right. So at this point, I think it is important to provide some context for this review. The AB 2588 statute does not explicitly require the SRP to review new chemicals for consideration under the program. However, we do feel that this is an important step in our process, because this list is an integral precursor to the work OEHHA does and then you ultimately review and approve.

That said, this consultation is new territory for everyone involved. Therefore, we have proposed -- prepared a number of questions that we hope will guide you in your review of the proposed new chemicals.

The first question is - and I'll go in more detail on the next couple slides about this as well - are we missing any important air toxic chemicals from the proposed list? Are the functional group characterizations for emerging chemicals appropriate and adequate? Are there other functional groups to add? Are there any chemicals on the "Not Proposed for Inclusion List" that should be included in one of the appendices?

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: All right. So back to the first question. As mentioned earlier, the AB 2588 statute specifies six source lists for CARB to review in compiling the list of Appendix A chemicals, and also gives CARB explicit authority to include other chemicals of concern. Several environmental health experts have expressed concern to us that many new chemicals are put into commercial use only to be later found to pose significant public and environmental health threats. They pointed out that it can be decades before emerging chemicals can make it into one of the six lists cited by the statute.

So they have urged CARB to take a more proactive approach and include emerging chemicals in the AB 2588 list. An example of a data source that we reviewed for emerging chemicals is the U.S. EPA's Significant New Use

Rules. In requesting this review, we are seeking your guidance on whether there are additional chemicals or chemical lists that we should consider adding to Appendix A.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Our second question pertains to the use of functional groups as the basis for adding new substances to the list. In the past, chemicals were added to the list as individual substances or as part of narrowly defined groups. In the proposed new list, CARB staff have proposed three broad functional group categories that include poly- and perfluorinated chemicals; derivatives and substituted versions of polycyclic aromatic hydrocarbons containing any halogen atom, such as chlorine, bromine, fluorine, or iodine; and any chemical containing the isocyanate functional group.

We are proposing that any chemical containing these functional groups should be listed in Appendix A-I because we believe it can be reasonably expected that they would have important health impacts.

We would like to get your opinion on this proposal, and also on any additional broad functional group categories that you may want to recommend for inclusion in Appendix A.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Our third question is whether any of the chemicals on the "Not Proposed for Inclusion" list should be included in one of the Appendix A tables. In reviewing the candidate chemicals, staff considered many factors that could contribute to their potential for public health concern.

For example, we looked at the chemical structure and other properties that can inform whether a substance can become airborne. We also looked at special considerations for heavier substances, such as how is the substance being used and whether it can become airborne as a result of its intended use or as by-product of a physical or chemical process.

For example, a substance created as by-product of combustion could become airborne even if it is not volatile at room temperature. We would like to rely on your expert opinions to make recommendations on any chemicals currently not proposed for addition that should be placed in one of the Appendix A tables.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Now, we'll focus a little bit on next steps and the process that we're looking at.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: As mentioned earlier, this consultation is new territory for everyone involved, and the format in which the Panel would convey the results of their review is not yet clearly defined. We would like to get written recommendations, in which you either express your scientific -- scientific acceptance of the proposed new substances or provide recommendations for additions or deletions to the proposed list, and also provide guidance on the appropriateness of using functional groups as the basis for listing groups of substances.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: In order to allow for adequate time for review of the proposed revisions and proper consideration of public comments, we are proposing a timeline that begins with today's Panel discussion, and which continues with a webinar on November 20th. We anticipate that at some point after the November 20th webinar, and if necessary early next year at the February meeting, the Panel might be ready to issue preliminary recommendations.

Final recommendations would be issued in late 2020 or 2021 after we report back to the panel on the outcome of our Board hearing on the regulation amendment.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: As for the rulemaking schedule for the emissions inventory criteria and guidelines amendment our aim is to start the public workshops on the proposed updates in early 2020. We anticipate taking the rulemaking package for our Board's consideration by late 2020, and will report back to you on any final changes to the proposed new chemical list after our Board hearing.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Public comments on the proposed Appendix A chemical list will be accepted as part of this review and the guidelines regulation amendment process. The comment period for the SRP review has been extended until November 8th, 2019. And comments received by this deadline will be addressed at the November 20th webinar. Comments received after this comment period closes on November 8th will be addressed as part of the guidelines regulation amendment public process.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Comments on the proposed new Appendix a chemical list should be emailed to Gabe Ruiz, who's manager of the Toxics Inventory and Special Projects Section to my right or to me at the email addresses shown on the screen.

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AQPSD ASSISTANT DIVISION CHIEF EDWARDS: As I conclude my presentation, I would like to put our questions for you back on the screen to provide a starting point for the ensuing discussion.

Thank you very much for your attention. And at this point, we'd be happy to answer any questions you may have for us.

CHAIRPERSON ANASTASIO: Great. Thank you very much, Dave. The first one, clarification and correction. The teleconference meeting we're going to have in November is November 22nd, not the 20th. So SRP members put it in your brain and on your calendar, it's the 22nd. It will be in the morning. Jim has already sent out the email with the day and time, but it's not the 20th.

Okay. Thank you very much, Dave, for that. I just -- I open it up to the Panel, comments?

Joe.

PANEL MEMBER LANDOLPH: Well, initially, just let me restrict my remarks to carcinogens. I teach this to the graduate students every year. And there is a million-fold variation in potency of carcinogens. So that we don't bankrupt the State, I think, you know, you should prioritize them in terms of those that already have cancer slope factors move them up to the top.

And, for instance, dibenzo[a,l]pyrene is more than 100 times more active than benzo[a]pyrene, which is already extremely active. So that kind of stuff you want to move up to the top, if you can.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Great. Thank you.

CHAIRPERSON ANASTASIO: Let me just clarify on that. I mean, the purpose of this list is to require facilities to report their emissions of these substances, right?

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: (Nods head.)

CHAIRPERSON ANASTASIO: OEHHA will make the determination what's the order in which substances will be tackled for whether it's a REL or a cancer potency factor. So we just want to make sure that things that make it onto this list are substances that we should be concerned about. And then OEHHA will do the prioritization of the order in which they get addressed.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yes, yeah.

PANEL MEMBER BLANC: So a question that would help us inform our input for you. The earlier slide which had the table of the new things on the list summarized by category was one of your earlier slides.

Yeah. So has the -- these are new, so these are not ones that are already toxic air contaminants, correct? I just want to make sure I got that part of it.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Correct, yes. These would be new proposed.

PANEL MEMBER BLANC: These are the new.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yes.

PANEL MEMBER BLANC: It would -- if these -- if the old ones, the existing ones, have already been similarly categorized or if they could be similarly categorized, it would rather interesting to see proportionally where are you adding more? Because this -- one -- you know, I suspect the reason there are very few metals on this list is because there are great many metals that are already regulated, for example.

But the neurotoxins, there may be relatively fewer proportionally that are already regulated. So would it help you see what the impact of this list is, in terms of how would it be changing the mix? Although, I will say that I absolutely agree with what was said earlier is it's rather confusing. Those of us who like Venn Diagrams in our heads, you know, we see these groups and it's sort of mind-boggling, because it's, you know, apples and oranges. An so it's -- it is hard to grasp some of it, right? I mean, most of the metals are neurotoxins, so I guess

they're in both categories, you know, that kind of thing.

So I just -- for what it's worth, some of this is based on human health effects and some of it's based on substance category. I mean you can imagine if you had something up there that was chlorinated hydrocarbon as a category how confusing it would be. So I'm not, you know -- I'm not convinced that this is necessarily -- this many groups is helpful. I understand why you want developmental and reproductive toxicants, because that has certain regulatory driving effects, as does the carcinogens.

But once you get to other things, I'm not entirely convinced. But anyway, just as -- I don't want to overplay that. But I would say it would be nice to see side by side, because it's -- you know, you -- if we look at a table like this, we have to bear in mind constantly, well, what's already listed? So it's not here, because it's not listed, not because -- it's not here because it's already listed, I'm sorry, not because you forgot about it or something, right?

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yeah. So we can definitely provide that to you, the breakout of the existing list and then sort of overlay that with this proposed list, so you can sort of see side by side. For example, metals, the number really is much larger based on

the existing list as well.

And then I'll also turn it over to Beth to kind of maybe give a little bit more detail. I'm sure she can talk a little bit about how that looks currently just.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR:

Yes. Thanks.

You're absolutely right. There are -- almost all of the typical metals are on the list already. In fact, we have cobalt, for example, as a single entry so far, but we will by expanding it in this round to more closely match the health values in the way they're structure, that it was just approved this morning.

But the other thing is just the categorization was -- is not something that we routinely do. It was actually kind of an outcome of the last meeting that we had with you folks in June. There was interest in saying we had it so that you could easily find which source list it came from. But there was interest, in at least several of these were named by folks that said, well, if I were going to kind of focus on my area of expertise on the list, I'd like it broken out by these. So we tried to just kind of follow the suggestions that were made.

And, yes, there are many other types of health effects that could have been broken out. But I think these were the ones that we heard from the panelists that

were maybe in -- areas of specific interest to someone, so we tried to do that.

But, yes, as Dave said, we could certainly follow that same pattern and apply it to some of the existing list chemicals as well.

PANEL MEMBER HAMMOND: Kathy.

As a chemist, I have to say don't we want to have other organics on the list. I mean, it's just an area that we need to -- now, I'm sure that organics are represented in the outcomes, but there might be organic chemicals that are suspect, so just kind of in a sense of completeness. So then at least that way we've kind of at least accounted for the chemicals, the sources, but -- and then from the other side, the -- there are these other health outcomes.

I mean, I think the point really isn't even -- I mean the categorization is -- is this really how they came to your attention? So, of course, we have these various carcinogen lists. And so that's how they come to be there as carcinogens, but they might -- they're either inorganic or organic, right?

And similarly, we now have Prop 65, so that also gives us the developmental and reproductive toxicants. So those are the kinds of things -- so we should recognize that. But meanwhile, it certainly should be true, if we

knew of pull -- we knew the pulmonary outcome led us to think of compounds. I think it would be good to think of the general outcomes we think of and as another way to try to be collecting.

In terms of the sources of data, just in terms of getting a -- making sure we have a complete list of what's known, another simple one, and maybe everything is already covered, but just to say have you looked at the ACGIH threshold limit values? I would at least want to make sure that we've included them all. They may -- they're like 650 or so of those. But it's just a list of if they've got -- if they've identified it, we probably want to include it.

PANEL MEMBER GLANTZ: Well, so I -- I miss -- I wasn't at the earlier meetings I mentioned. And when I tried to look this over, I was like totally overwhelmed.

(Laughter.)

PANEL MEMBER GLANTZ: But you know one thing you might want to do, because the master list is in an Excel spreadsheet. And you might want to have us add a couple columns, like one is outcome, one is chemical class, and one is source of where you got it. And then if you have that in your master list, then you could generate the three tables, one where you stratify it on each of those things. And then the person, depending if you're like a

biologically oriented person or a chemist, then you just look at the different lists. So that might help make it a little less scary.

PANEL MEMBER BESARATINIA: Yeah. I'm just wondering about how practical it is to require reporting of some of these chemicals or substances that have been identified in Appendix A-I. For example, environmental tobacco smoke or secondhand smoke this is a complex mixture of several thousand chemical containing toxicant and carcinogens. So each one has a different type of effect.

So in these cases, are you going to measure the prototype or a representative compound from this whole complex to use it as an index? It's kind of confusing to me how that is going to be done.

And the second point is that -- well, by definition every smoker can be a source of ETS or secondhand smoke. What -- are you going to like narrow it down to establishment where smoking is allowed, for example, casino or -- it's kind of confusing.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR:

Okay. Let me provide a little context. So this list is a part of the Air Toxic Hot Spots Program, AB 2588. And the program is focused on facilities, industrial facilities and commercial type facilities, that

are -- the first step is to determine whether they are subject to that program at all.

So there is a set of applicability criteria that are applied to that facility. And so generally speaking, we're talking about emissions from large industrial type sources, some smaller things. You can have smaller gas stations, auto body shops can also be sources without being large industrial type of application.

But the first step is determining that they are, in fact, subject to the Hot Spots Program. And then we also have exemptions in -- built into the emission inventory regulation that this is a part of. And those exemptions are for like personal use by their employees of products, for example. So generally speaking, the smoking that their employees might do is not part of what was intended to be covered by the statute.

So the statute is pretty clear. It starts with large facilities that emit a lot of criteria pollutants. It steps its way down from a 25 ton facility to a 10 ton facilities. And then it asked ARB to identify other classes of smaller facilities that should be a part of this program.

So that's where we identified things like gasoline stations and auto body shops, and dry cleaners, and small chrome platers, things likes that. But that is

the first step, they have to actually be a facility subject to the program before they would even address this.

So as it turns out, the main reason why you'd ever have a situation with say environmental tobacco smoke or tobacco smoke at all, we did recognize there are a few facilities that actually do testing and actually have smoking machines. So in a case like that, they might actually have to report these emission. But by and large, most of the other situations would probably be covered by one of these personal use type exemptions and would not be something that the facility would be trying to quantify.

PANEL MEMBER BESARATINIA: What would they report? What would be the unit of measure in this case?

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: I don't know that one has come up yet for sure. I don't know that one of these facilities that we had sort of heard about has actually come subject to the program. It would be in pounds basically, pounds of that substance. It would not necessarily then be speciated. We could do that as another step. We could try to break it out using existing literature. But at this point, if they would just report the pounds of that substance, they would have met their reporting requirement. And then we would think about what we needed to do or what would -- what we would

like to do with that data in terms of a further breakdown into components.

PANEL MEMBER BESARATINIA: Thank you.

PANEL MEMBER KLEINMAN: Just going down your list, I noticed that you have several of the carbonyl type compounds that are currently very popular flavors for vaping, benzaldehyde, diacetyl. And I would suggest that you might want to bundle some of the -- you know, those up as you start to consider whether you want to look at potential risks from these things.

That may be a -- you know, another way to categorize, so cinnamaldehyde, vanillin, benzaldehyde, diacetyl. I saw a couple of others. You've already earmarked them. But maybe if you look at them as a group, there may be a large aggregate.

CHAIRPERSON ANASTASIO: Do Panel members have any answers to Dave's first question? Are they missing any important toxic chemicals from the proposed list? Are there chemicals that people -- maybe some of you favor toxicants you checked, you noticed they're not the list. Anything in category one?

PANEL MEMBER BLANC: One of the problems is kind of what I was alluding to, which is we'd have to have at our fingertips what's already listed.

CHAIRPERSON ANASTASIO: Well, so Dave did send --

PANEL MEMBER BLANC: No, I understand, but it's not -- you know, I mean, I focused on this list not on the list of, you know, the -- what is it 600 or how many you have currently listed?

CHAIRPERSON ANASTASIO: Right. Yeah.

PANEL MEMBER BLANC: So that's one problem.

But -- so it may not be something that, you know, efficiently can be done sitting here in front of you, you know, what -- what is missing. But I think you've heard a couple of good suggestions. Kathy said, you know, look at the ACGIH list and just make sure that there's nothing missing from there. Look at the NIOSH handbook of chemicals. These are workplace ones, but still gives you a sense. Most -- ACGIH is actually more comprehensive than the NIOSH list. But I doubt there's anything on the NIOSH list that's missing from the ACGIH, but I can't say that for sure.

You might also look, there's a -- it would be a useful table to you that's in the Olson Toxicology Handbook. Kent Olson has a very large table of toxic materials. Now, many of those are not airborne. It includes, you know, other things that would be irrelevant, but it's -- the industrial chemicals there would be a good place for you to look and make sure that you, for example, got -- well, a technical question. Since you're

considering -- and this addresses one of your other questions. You're going to take a sort of group approach to isocyanate variance. So you're not going to necessarily have to list everyone of them individually, is that the idea there?

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yeah, that's the idea there.

PANEL MEMBER BLANC: Yeah, I think that's a -- if you want my feedback, that's a clever idea. You might also consider the parallel reactive chemicals that are in epoxy mixes, which are called -- what's the best way of summarizing those? In the epoxies, the -- but you know there are a bunch of different --

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Like the resin monomers, is that what you're getting at or...

PANEL MEMBER BLANC: Well, it's the ones that react with them, acetyls or something, I don't know.

Yeah. Those are a couple of examples.

PANEL MEMBER HAMMOND: I mean, I totally agree with the concept there. But, you know, the epoxide -- the various epoxide and isocyanate compounds, which by the fact that they're reactive in terms of chemically for the purposes of an industrial purpose, they're also very reactive with human tissue.

PANEL MEMBER BLANC: So, for example, today, this morning, we had this -- I notice you put a bunch of cobalt compounds, even though cobalt is already listed as just cobalt metal, right? That's correct?

So would it save time -- I mean, is your -- couldn't you take the same approach then with metals that have various salts and various organic things that you didn't have to like list five different cobalt subspecies --

PANEL MEMBER HAMMOND: I think we need to be careful with that, because as they -- we saw in cobalt, there was a huge difference in the toxicity.

PANEL MEMBER BLANC: Well, they could say --

PANEL MEMBER HAMMOND: And certainly nickel that's true of as well.

PANEL MEMBER BLANC: They could say -- they could say soluble cobalts and -- and so, I mean, I don't -- I'm just saying because you're going to miss, right? There are going to be other ones that you're -- so you're either going to have to clutter up your list with lots and lots or if there's a way -- if there's shorthand.

But anyway, that wasn't what I was about to say. What I was going to say is this morning at our discussion, it came out that tungsten cobalt --

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR:

Yes, we heard that.

PANEL MEMBER BLANC: -- tungsten carbide cobalt, or a.k.a. hard metal, which is more carcinogenic than cobalt -- unless that's already listed as a TAC, which I think it isn't?

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: We heard that and we will be considering adding that.

PANE MEMBER BLANC: It's not on this list. That's an example.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR:

It's not there yet. We heard it this morning.

PANEL MEMBER BLANC: Okay.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR:

May I comment just a little bit on that? So we're walking kind of a balance here between saying if we know about specific compounds that are in commerce now, it is sometimes an advantage to list them explicitly, even if it means kind of expanding under a group, because if we can include their chemical abstracts registry number, their CAS number, that facilitates an industrial source who might be looking through their material safety data sheets realizing that, yes, that is a listed chemical. And if we don't do that, we run the risk that someone who's maybe, you know, a technician at that facility doesn't have the chemistry background, doesn't realize

that this thing that they see on the MSDS that has a slightly different name, really is a part of that group.

So what we have been -- this balance that we've tried to strike in the past has been that when we are aware of fairly commonly used explicit ones, we would try to put them on the list and include that CAS number, because it makes easier. We provide that list electronically. People can go through -- an industrial facility can go through that list electronically, if they would like to.

But then the balance is that that means that if something is emerging, we might not have it yet and we'd have to go through a regulatory process. So that's the purpose of these three functional groups. We are saying that probably anything that contains those chemical functional groups, there's a reasonable probability that they would be having human toxicity concerns. And so we feel that that whole group could be considered as a new class. And then it's up to the facility to tell us a little bit more about what those chemicals are, rather than us having to already have figured out every single one. Does that -- does that answer your question?

PANEL MEMBER BLANC: That sounds great.

PANEL MEMBER KLEINMAN: This is more for my edification. But I was looking at the list of not

proposed and I noted that you had wood dust listed. And it's indicated wood dust is a IARC 1 carcinogen. And it says should just report particulates. And I think that may be an oversimplification, because if I remember right, not all wood dust is a carcinogen. But some of that which is not a carcinogen is a very strong allergen and is certainly related to occupational asthma in the woodworking industry. So I think that might be something that could be looked at with a little more specificity.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: We've had similar discussions with our colleagues at OEHHA and tried to grapple with that same kind of question of where -- where would we go with this in terms of whatever -- would a health value ever be adopted for a thing called wood dust? So it's a challenge. And any guidance you have on that would be definitely appreciated.

PANEL MEMBER KLEINMAN: Yeah. The ACGIH TLV Committee went into this in great detail. And I might be able to put you in contact with those folks.

MS. SCHWEHR: Great. Thank you.

CHAIRPERSON ANASTASIO: Beate.

PANEL MEMBER RITZ: I just want to make you aware that there is a big push right now to generate exposome data. And just in September, there was actually a publication in Environmental Health Perspectives by

Barupal and Fiehn - Oliver Fiehn from I think UC Davis - on all of the chemicals that they were able to cross-link between different databases, including PubMed articles. And that might actually be a great resource to just check against. Because if it ends up in the blood, they look at the blood exposome. We know that people are exposed, right?

Maybe -- maybe it's not a health effect, but they are linking all sorts of databases and you could at least us it as a tool.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Great. Thank you.

PANEL MEMBER LANDOLPH: For carcinogens, I would certainly recommend taking all the IARC Class 1 carcinogens, which are known human carcinogens, and the Class 2, which are probable human car -- 2A, which are human -- probable human carcinogens. And a lot of these have been picked up on the Proposition 65 list. OEHHA knows all about this already, the CIC, Carcinogen Identification Committee.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Thank you. Yes, we've tried to make sure that all the Class 1s and 2As are somewhere on the list. In some cases, they didn't end up on Appendix A-I to be quantified, because they may not have met that second

criteria of whether they're likely to become airborne.

Some of them, for example, are oral pharmaceuticals. And so that's where we tried to put them into some place like Appendix A-III, where if you are a manufacturing facility, you're handling as you're making it, might result in some fugitive emissions. So a manufacturing -- manufacturer of that pharmaceutical could be subject. But if you are just using that pharmaceutical at the point of end use, and it's a pill or something like that, it's not -- or an injectable -- there's even some of those in the IARC Group 1s -- we wouldn't necessarily want that on the Appendix A-I for an industrial facility to try to quantify.

PANEL MEMBER HAMMOND: Kathy.

I'm going to propose -- or I'll ask a -- the question first. But to what degree does ARB, stepping back, actually do any sampling to do any kind of validation of the emissions data that they've received from the facilities? And my guess is probably not very much.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: So as a part of --

PANEL MEMBER HAMMOND: I have a follow-up to that.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR:

Okay. As a part of the emission inventory guidelines, of which Appendix A is one of the appendices, there is another appendix, Appendix D, as in dog, that is a list of source types for which we are actually requiring source testing, airborne source testing to be done.

PANEL MEMBER HAMMOND: By the company and where?

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: By the company.

PANEL MEMBER HAMMOND: Where is the testing? Is it stack testing --

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Yes. Usually, it's --

PANEL MEMBER HAMMOND: -- or fenceline or --

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: It's usually a stack type of test. Yeah. So for example, there would be -- the catalytic cracker at a refinery is subject to a source test --

PANEL MEMBER HAMMOND: Um-hmm.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: -- because we don't think there's really any other way to get reliable quantitative data. So at the beginning of the Hot Spots Program way back in the late 80s, those tests were conducted. And then ARB collected that data and developed emission factors based on that actual source testing, so that is now a pool of resources

that other facilities might be able to use if they're similar enough.

But, yes, in some cases, we actually said source testing is probably the only reliable method to quantify some of these.

PANEL MEMBER HAMMOND: So I guess I think it's important as we go forward -- I mean, just making longer lists of chemicals -- I mean, first of all, I do want to acknowledge that this is a lot of work and I'm appreciative that you're doing it. Let me be clear.

But I think we also need to think about how that would be used. And so making sure -- rethinking again, maybe it's time to retest with all the various air pollution devices. It may be time to retest, because there are new chemicals that we're talking about, which may be bringing in new facilities. And maybe at a certain level, you know, X percent, three percent even, something like that, some percent that ARB does some testing to validate what the companies have done and maybe some also community level testing to see what's actually making it into the -- I mean, I think you're right, stack testing tells you something about emissions. But also then going out and seeing what's -- what makes it to the fence line or to the community. But I think that we need to take a more holistic view of this whole process.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Just one thing to add on that, the sort of that -- the audit capabilities. I'm not sure how much it exists in the Hot Spots Program, but our new reporting regulation - I think I talked to you guys a couple -- maybe six months ago on that, our criteria on toxics reporting regulation to get annual data on this as opposed to the every four year, which is limited in the Hot Spots Program, there is a sort of audit verification component, where we could go in -- where we do at least have the authority that was in the Health and Safety Code to go and evaluate whether they criteria on toxics data that was submitted by a facility was accurate.

So that capability does exist. We haven't explored that a lot yet. I mean, we're still working on just trying to get applicability, like who has to report in, but that it --

PANEL MEMBER HAMMOND: I mean, you have that authority now you're saying or you haven't explored whether to get --

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Just came in like two years ago.

PANEL MEMBER HAMMOND: Oh, you just got it, so you haven't actually exercised that yet?

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Correct,

yeah.

PANEL MEMBER HAMMOND: Yeah, I just -- I think making this part of the planning would be an important piece, that's all. But that sounds like it is partly.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yes.

CHAIRPERSON ANASTASIO: Any other comments related to Dave's first question, any missing important air toxics?

Yes, Mike.

PANEL MEMBER KLEINMAN: You may have done this, but I'm wondering if you've cross-referenced the AB 617 locations and the con -- and the emissions inventories that were used to help select the cities that are involved or the communities that are involved. And that may -- you know, if there was any of those that you're missing on your list, that would be useful to have. Also, it might be a strategy for which ones you want to look at first.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR:

Yes. I think to the extent that most of those inventories we're relying on the 2588 data from before, we have done that. And then I think one of the comments that came up last time was a great suggestion that we ask if there were anything else in those communities that we did not yet have, and we went through that process, and we did identify a couple of extra pesticides based on that

review.

PANEL MEMBER KLEINMAN: Great.

CHAIRPERSON ANASTASIO: Yes, Joe.

PANEL MEMBER LANDOLPH: And I was thinking on the carcinogen list, there could be certain chemicals that might be starred as of particular importance, even though they're already Category 1, I'm thinking of 2,3,7,8-tetrachlorodioxin, because it -- the data from Seveso, Italy showed that it raised the cancer rates in almost every organ in the body in Italy in the people who were exposed to it. And arsenic, which is like a -- oh, carcinogenic in five or six different organs. So things like that, which are multi-system carcinogens might be --

PANEL MEMBER BLANC: But, Joe, those would all -- those are already listed. I mean, those are not -- they wouldn't be the --

PANEL MEMBER LANDOLPH: Yeah, I said they're listed as Category 1.

PANEL MEMBER BLANC: No, but I mean they're already listed.

PANEL MEMBER LANDOLPH: Oh. Okay. Good.

PANEL MEMBER BLANC: They're not here because they're already --

PANEL MEMBER LANDOLPH: Good.

PANEL MEMBER BLANC: They're already.

PANEL MEMBER LANDOLPH: Good.

PANEL MEMBER BLANC: I don't want to -- I won't stake my life on it, but I'm pretty sure --

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Yes. Those have been in the program for quite some time. Yes, that's correct.

PANEL MEMBER BLANC: Right. So the -- you know, it's a little bit like, you know, Claude Rains in Casablanca rounding up the usual suspects. I think what they're asking is that, you know, if we think outside the box, what is it that we're not thinking of, I think? Is that -- is that correct?

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yeah. Yeah, I think that gets to that functional group category. It also gets to the -- like, for example, we mentioned the significant new use list that EPA puts out. Sort of the -- just because as you sort of saw just from the background, this regulation has been really updated twice in roughly 25 years. So the opportunities that we do get to go into this are few and far between. So right now, we do have an opportunity to kind of go in and try to at least be proactive in how we're doing everything, as opposed to reactive, which is sort of looking at where the potential for development lies and what sorts of chemicals may be coming out or functional group relevances may be

coming out in the future as well.

CHAIRPERSON ANASTASIO: So I second Paul's point about it's hard to figure out if a toxicant you're interested in is already on the other list. But, you know, you go into the PDF, you do control F, you write it in, and you see if it's there. So you caught all the ones that I could think of initially. They're either on the original list or on the new list.

But I encourage other Panel members, if you have some favorite toxicants, just check, see if they're on the old list, see if they're on the new list. And if not, let's discuss it at our November 22nd meeting.

I was trying to think of what might emerging contaminants in California look like. So I was trying to think of emerging industries. And one of the ideas that occurred to me - it may sound crazy - was cannabis, right? A lot of cannabis cultivation in California, not a lot of cannabis processing. So I'm wondering are there -- I know there are complaints about odors from cannabis operations. And so I'm wondering if there are actually cannabis-specific toxicants that we haven't been thinking about that might actually be important. So I would encourage you to see if there's any literature on that, and perhaps there are some compounds.

Now, I know that in your do-not-include list, you

had -- some things were excluded because they were botanicals or natural. So it makes me wonder is -- if there was a cannabis air toxicant, would it be listed or is it natural?

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: I don't think that our exclusion of a botanical is an automatic.

CHAIRPERSON ANASTASIO: Oh, okay.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: It's more that we looked at them and thought about how they would -- how could they become airborne, was that very likely in the way that they're used, and things like that. And you're right, with cannabis being more of something that is vaporized or combusted, it might be different.

CHAIRPERSON ANASTASIO: And I wasn't thinking of cannabis use, but more the processing to the point where it gets to the consumer. So, you know, some of these farms are quite large. And I know that there are a lot of neighbor complaints in some cases. And so there may be some real issues there.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: John Budroe.

DR. BUDROE: John Budroe.

Well, one question, for example, an indoor grow

house or a greenhouse that's growing cannabis. Is that an ag use? And ag uses are generally not covered under the Hot Spots Program.

CHAIRPERSON ANASTASIO: Right. But that would be the application of a chemical to the crop, right? I'm wondering if the crop emits something itself.

DR. BUDROE: No, we're talking about there are complaints that do come from indoor greenhouses or indoor growing areas that is pungent.

CHAIRPERSON ANASTASIO: Yeah.

DR. BUDROE: So -- and there are probably -- the plants are emitting volatile chemicals. But, you know, the question is, is that still -- that's an agricultural production area. So is that covered under Hot Spots?

PANEL MEMBER BLANC: But just carrying it one step further, we had an extensive SRP review of secondhand smoke. And we -- we -- our findings led to its determination as a toxic air contaminant. So I suppose secondhand marijuana smoke might be an exposure that, at some point, could be considered.

And another -- no, go ahead, John.

DR. BUDROE: That could potentially be so. But what we're really talking about here is the actual growing facilities.

PANEL MEMBER BLANC: No, I understand, but it

triggered me thinking that --

DR. BUDROE: Okay.

PANEL MEMBER BLANC: -- one thing that's not on this list -- because secondhand cigarette smoke shouldn't be on this list, because it's already -- already been considered, right? So -- but we've never considered secondhand cannabis smoke. So that's one thing.

Another thing, thinking back to previous discussions that this Committee has had, we had, you know, a very, very involved review of diesel exhaust. But my memory is that what we designated was diesel exhaust particulate and that we never did designate diesel exhaust gaseous material.

PANEL MEMBER HAMMOND: But it's on the -- it's on the list now.

PANEL MEMBER BLANC: So that's --

PANEL MEMBER HAMMOND: Yeah, I was going through the list. So I was surprised to see that and pleased.

PANEL MEMBER BLANC: So that's a good --

PANEL MEMBER HAMMOND: Pleased to see that.

PANEL MEMBER BLANC: So the system worked, whatever your -- I mean, that's an example of something that slipped by. So if you've caught that -- however it was that you caught that, good thing.

PANEL MEMBER HAMMOND: Yeah, that was -- that was

good work. Trying just another thing, has anyone ever compiled a list, thinking of these big spreadsheets that Stan's been talking about, a list of the chemicals how many facilities in California respond and say they have emissions? And that actually might be some really interesting things to start bringing those data together, and looking at what we have, and looking at -- has that been done, or if not, maybe we could think and put that on the agenda.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: That is one of the things that is an outcome of the AB 2588 process, is that these -- these facilities finish their reporting. It's reviewed by the district, and then it's forwarded to CARB and it resides in a database that we have here. So for all of the facilities that have been subject to the Hot Spots Program, we do have what they've reported as their emissions.

In fact, I looked up, after I heard your discussion on cobalt, I was looking to see how many reported facilities. We have about 200 facilities that have reported just generically cobalt. We don't have the breakdown of the soluble and insoluble yet, of course, but we do have some.

PANEL MEMBER HAMMOND: And is that publicly available so people can do that?

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Yes. Yes, it is.

PANEL MEMBER HAMMOND: Oh. Okay. Great. Maybe you can later send that around. That would be great. Because that -- that would be a great MPH project, you know, just to actually look. Has anyone actually looked at that as a totality and kind of have you been able to do that?

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Yes.

PANEL MEMBER HAMMOND: Oh, good.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: We get lots of data requests from researchers to look at that database.

PANEL MEMBER HAMMOND: No, but I'm wondering has anyone compiled that to look at, okay, what do we know now? Has anyone really taking a sys -- taken a systematic view of some of that that we know?

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: We've done a number of analyses. We also have a mapping tool that helps people see on a map --

PANEL MEMBER HAMMOND: Uh-huh. Okay. Okay.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: -- where facilities are. You can ask for it by a specific chemical.

PANEL MEMBER HAMMOND: So like where are all the cobalt places and we could -- they'd pop up?

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: I don't know if we have cobalt on the map quite yet.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Not yet. Not on our map. But if you did a data request --

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: A data request would list it.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: -- we'd give you a list of the 200 facilities by county, zip code, address, and emissions.

PANEL MEMBER HAMMOND: And how the emissions are.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: (Nods head.)

PANEL MEMBER HAMMOND: Great.

PANEL MEMBER GLANTZ: Well, so if I could just go back to the -- and this may be more a question for lawyers than scientists. But, you know, if you've got a marijuana grow out in a field somewhere, that's agricultural. But if you're in a city and you've got an industrial greenhouse facility, that's, you know, then emitting stuff into the air outside the building, I mean, is that considered agriculture or does that now become an industrial thing, which would be regulated ARB, in terms of the emissions that make it out of the building? Does

that -- you know, Cort is right, I mean, people are complaining about that. And if you can smell it, it's probably not a good thing.

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yeah. I think that is a discussion that we probably do need to have internally with our lawyers in the room to talk about sort of what is the extent of scope and authority that 2588 gives us to get into that -- into that category specifically.

I do agree with you that there is some distinction between a crop going in a field and a crop growing in an industrial building and how the permitting structure works, what the classification is within that district as to how they class that type of activity, because especially if it's indoors, it's a lot of back-up, it's a lot of generators, it's a lot of more industrial type sources that might be being used.

I think one other piece to kind of maybe add an extension on to think about potentially is also the processing site, because outside of the ag use side, then there's the actual processing of the plant. And that could have some also implications as well. So there's -- that's I think -- that is, I would strongly say, is in the Hot Spots Program. The growing piece is I think a gray area.

PANEL MEMBER BLANC: So --

PANEL MEMBER HAMMOND: One of my students just did an ergonomics project on the ergonomic problems. And there are a lot as it turns out in cannabis industry. But look at the pictures that he had showing that, made me realize this was an industrial process as well.

PANEL MEMBER BLANC: So coming back to functional groups and categories. How are you dealing with the myriad of fluoro -- fluorinated carbons? You know, I mean, every different combination, they all have -- you know, all the freons, have you -- how have you dealt with that? Freon 123, freon 124, freon -- you know.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: We have I think it's a handful of the chlorofluorocarbons right now on the list, just a limited number, because those are the ones that had exhibited enough toxicity to be on one of those six source lists that Dave mentioned during the slide presentation.

The others have not emerged as on the radar of these organizations, international, national, and local, that look at toxicity health effect type of things. So those have not -- we don't have a lot of the freons on the list. We just have a handful on the toxic list. They're handled in other programs here at ARB, of course.

PANEL MEMBER BLANC: Right.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR:

But as far as the toxics program, there's only a handful that made it. Now, that's not counting these per- and polyfluoroalkyl substances that are analogs to like PFOA and PFOS. Those we're trying to capture in two ways. We'll have a long list. I think we have something like 70 of them. Let's see, how many did we have of those?

Yeah, about 74 individual ones that we've been able to identify from known literature. But then we are also creating a functional group to try to get ahead of the emerging ones.

PANEL MEMBER BLANC: Yeah. That's an area --

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR:

But are you asking specifically about the -- just like the freon refrigerant type ones?

PANEL MEMBER BLANC: Both, I think.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR:

Both. Okay. Yeah, so --

PANEL MEMBER BLANC: And see it gets a little bit more complicated because in addition to the sort of classic long-chain polymers, there are also these fairly short but not monomer polyfluorinated materials that are used as water repellant coatings and have had a lot of human health effects. So it's complicated. Complicated chemistry, but it's also complicated to capture them, I

think, because they keep switching around --

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Yes.

PANEL MEMBER BLANC: -- and, you know, they're not -- and that -- so that's a good candidate for a group -- functional group approach I would say.

CHAIRPERSON ANASTASIO: While we're on that topic, do other Panel members have thoughts about other functional groups that should be considered? I think the approach is great. You know, that was one of your questions, is this a good approach. I think it's great, because right, it's -- otherwise, it's whack-a-mole all the time. You know, you add another CH2 group and it's a different compound. But if you've got the entire class, then you capture that.

So are there other functional groups that Panel members can think of that should be included?

PANEL MEMBER BLANC: Well, you know, methylating agents are not great things, in general. But I don't -- beyond that, I don't have a specific

PANEL MEMBER HAMMOND: Aldehydes. We certainly know a lot of them are probably are -- I'm sure are already on the list. And that's actually one of the big things in the diesel exhaust, but you might add that. And I think there -- you know, for some of these groups like

aldehydes, sometimes you can have reactions that kind of capture a class as opposed to just doing individual compounds, if you just get a chemical reaction for the functional group and get a total, without necessarily having to identify them all.

PANEL MEMBER BLANC: And also, as a group on your metals that you've added -- have you -- I haven't gone through here with an eye towards it, but rare earth metals. Have you considered them? I doubt they're already on -- cerium, lanthanum.

Also, in terms of the metals that are in catalytic converters that there's been some issues about, like ruthenium, and platinum, and palladium. You'll have to double check, but I'd be surprised if they were already --

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Most of those are not yet on the list.

PANEL MEMBER BLANC: But maybe they're -- not on the old list, right now.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Not on the old list. No on the old list either. Good suggestions. Thank you.

PANEL MEMBER BLANC: To clarify too, I saw that you have a bunch of beryllium compounds on the new list. Is that because the old only just had beryllium

generically and this was an example of you trying to get specific CAS-associated entities?

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: That's right, where we had some, but we're adding additional ones.

PANEL MEMBER BLANC: Okay.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: And you -- we put a little "e" in the column on the spreadsheet, so that you can tell. What we tried to do is bring the group together so that you could see it in context.

PANEL MEMBER BLANC: Right.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: But the "e" are existing ones.

PANEL MEMBER BLANC: Gotcha. Gotcha.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: And then without the "e" were -- are the ones that we're adding additionally.

PANEL MEMBER BLANC: Yeah.

PANEL MEMBER HAMMOND: I have to say this is kind of amazing an overwhelming to me what you're trying to do here. But I think it's really great to step back and not just be in our old world all the time.

But just another list I thought of is maybe the EU banned -- you know, looking at the EU REACH chemicals

that achieve a certain status there. And I'm not sure how I would divide that. But at least look at that as a source to think about.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: We did pick up some from that, but I'm not sure it's been a comprehensive look at that.

PANEL MEMBER HAMMOND: Systematic.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Systematic, um-hmm.

PANEL MEMBER HAMMOND: Yeah, I think, at this point, I would add that voluntarily, you know, to your list of to always be paying attention to.

CHAIRPERSON ANASTASIO: I had one comment on functional groups. So you've got halogenated PAHs, but I'm wondering about other classes of PAHs, nitro-PAHs, polycyclic aromatic quinones. Certainly, they are toxic. And I don't know if you just hadn't considered it. I mean, some of them are secondary, right, formed in the atmosphere. But I suspect that there are emissions at least of some of those different types of compounds.

PANEL MEMBER RITZ: You asked for some favorite chemicals. I couldn't find the strobins, azoxystrobin, the fungicides, that you'd not only find in the fields but actually in drywall. They're are -- they are in what's called purple drywall. And from a few years ago, I

remember that they're extremely neurotoxic -- toxic to neurons in the dish at least, so -- and they seem to be coming up to be quite widely used, including in homes.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: And could you repeat the class again?

PANEL MEMBER RITZ: They're called strobins, azoxystrobine, S-t-r-o-b-i-n, I think, but they have all sorts of names that end with strobin.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Thank you.

PANEL MEMBER RITZ: Fungicides.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: Thank you.

CHAIRPERSON ANASTASIO: Okay. How about we move to the third question in Dave's presentation then. If people had a chance to look at the list of not proposed for inclusion and are there compounds that are listed there that, in fact, should be listed in one of the prior appendices? Any input on that?

I can maybe start it off. So I noticed it seemed that one of the criteria was vapor pressure. You know, is something volatile or not? And if it's not volatile and you couldn't imagine a dust-generating activity, it seemed that it didn't get listed. But it does seem, if you look at what's measured in the atmosphere, for example, you can

find cocaine in particles.

And cocaine is fairly non-volatile. But I think it's volatile enough that it can partition to the gas phase and then stick to a particle. So I would consider your volatility range maybe. And some of these things that are relatively low volatility are volatile enough that they can actually get up there and then partition to particles.

So I don't know if you had a hard rule for vapor pressure, but you may want to expand that range.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR:

Yeah, we didn't have hard one. We looked at the combination of the number of carbons at times, the boiling point, the vapor pressure, all of those things and tried to in that talk among staff and try to understand what we thought it would behave as. But that's a good point. Thank you, yeah.

PANEL MEMBER HAMMOND: Yeah, I had -- actually had been thinking about that too. I think that dust, in general, specifically if they're in small sizes, you know, if they're under PM10 really that they get transported. And so volatility is important, but it -- but I think as long as the particle size is small, it's going to be transported and should be included.

PANEL MEMBER KLEINMAN: Now, that you mention

that, nanoparticles in general might be a category to look at. But things like carbon nanoparticles, you know, nanotubes, nanofibers, those are in heavy industrial use now, so they may warrant being on the list.

AQPSD STAFF AIR POLLUTION SPECIALIST SCHWEHR: And we did pick up, I think, one or two examples of that that came from some of the IARC or other sources. We did pick up a couple of those. And, yes, if anyone else has ideas on a way to structure or categorize them, we'd be open to that guidance as well. So far, we just took the way they were structured on other -- one of these other six lists.

CHAIRPERSON ANASTASIO: Any other Panel comments on the third question or any of the other questions?

PANEL MEMBER BLANC: Cort, I have a methods question, technical question. So suppose a week from now, I have a chemical that I, you know, thought about and double checked and it's not currently listed and it's not listed here. Is there one person -- you know, should we be feeding those to Jim or -- so they don't have to hear from a bunch of different people. It can be sort of collected together. Is there a conduit for such comments?

CHAIRPERSON ANASTASIO: So if you have that information between now and November 22nd, bring it to our November 22nd meeting. So, you know, we will be meeting

again to discuss this list. And we expect some public comments about this, and so we will -- we'll get those public comments I think a week or two before the meeting. So we'll have some time to look at the public comments as well.

So we'll have a discussion of public comments, and any other ideas that panel members have about the three questions that Dave asked. So please between now and the 22nd, look at the those three questions, think about your favorite chemicals or your least favorite chemicals, and see if you have input on Dave on the three questions.

After the 22nd, how should we get input to you, Dave?

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: So I'm sort of envisioning the 22nd we'll have some public comments and then additional feedback from you all. As far as -- what we kind of -- what we're sort of envisioning is we are going to have a whole other separate public process when we do our regulatory update. We'll have public workshops, sort of initial comment, formal comment. So any additional comments could just sort of be submitted probably to Gabe or myself. And then we would incorporate those into our -- our informal comment that we have during the -- during that rulemaking process.

I think also as a sort of final step, what we'll -- after sort of hearing the different comments today, I think sort of in the recommendation piece, we'll have sort of a -- the action item list that we were sort of our -- in a sense, our homework to do in establishing a more comprehensive list, we can kind of talk about sort of recommendations where this, this, and this, and those were done. And then kind of write that up in a more formal way that may be at the end of the November discussion or the next meeting we can have some sort of a vote or something, whatever that equivalent is for this group. Does that sound --

CHAIRPERSON ANASTASIO: Yeah, we can certainly talk about what that would be. But it would seem to me a list of the SRP comments maybe enough --

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yeah.

CHAIRPERSON ANASTASIO: -- not necessarily having to vote as a group about --

AQPSD ASSISTANT DIVISION CHIEF EDWARDS: Yeah, I just wanted to -- I mean -- my Board is used to voting.

CHAIRPERSON ANASTASIO: Well, we'll see how people feel about voting on the 22nd.

Any other comments from the Panel?

Okay. So I've got a couple more small agenda items, but I wanted to give Jim a break.

THE COURT REPORTER: I'm fine.

CHAIRPERSON ANASTASIO: Oh, he's -- okay. Jim's a superman. He's going to continue.

So just first thank you to Dave, Gabe, Beth for all your input and for giving -- allowing us to give you input.

The next agenda item is administrative matters. So, the first is for me to remind you that we're going to have the conference call on the morning of the 22nd.

And then --

PANEL MEMBER GLANTZ: Do we have a time yet?

CHAIRPERSON ANASTASIO: Didn't we have a time or no.

PANEL LIAISON BEHRMANN: We have not set a time yet.

CHAIRPERSON ANASTASIO: Ah. Okay. Thank you. So --

PANEL MEMBER GLANTZ: It would be really good to set the time --

CHAIRPERSON ANASTASIO: Yeah, 100 percent.

PANEL MEMBER GLANTZ: -- because everybody wants -- you know, so we can get it on our calendar.

CHAIRPERSON ANASTASIO: You want to set the time right now?

PANEL MEMBER GLANTZ: That's fine with me.

CHAIRPERSON ANASTASIO: Or you want Jim to send an email right after the meeting?

PANEL MEMBER BLANC: Send an email.

CHAIRPERSON ANASTASIO: I think an email might be more efficient. But I hope everybody has blocked out the morning. That was what -- the email originally said, you know, it would be the morning of the 22nd, so --

PANEL MEMBER BLANC: Well, I have -- I have a half hour that was pre-booked and I can't change, but that happens, but before this was set.

CHAIRPERSON ANASTASIO: Will that work for you Jim?

PANEL LIAISON BEHRMANN: Yes.

CHAIRPERSON ANASTASIO: Okay. So Jim will send out and email. We'll nail down the time. Then the next meeting that we will do in person will -- it's tentatively set for February 27th, 2020. So make sure that's on your calendar. And Jim has already sent out an email about that as well.

PANEL MEMBER BLANC: February what?

CHAIRPERSON ANASTASIO: 27th.

The next administrative item, update on HDI, right, hexamethylene diisocyanate we considered at our March 2019 meeting. The REL for that has now been completed and adopted by OEHHA. So that's set. Thank

you, Panel, for all your work on that.

And that brings us to our last agenda item, which is both happy and sad. Happy for Jim, sad for us. So, Jim Behrmann is retiring after more than 20 years of service to the SRP and to CARB. So I know as Chair, I'm going to miss him enormously because he's the one who actually knows what's going on.

But we have somewhere -- well, do we have Reid?

We do not have Reid. Okay. Reid has something on his person that I need, which is a letter of appreciation for Jim and all his service. So we're going to send out some scouts?

No.

I'm going to ask Jim if he can get in touch with Reid --

(Laughter.)

CHAIRPERSON ANASTASIO: -- so that Reid can give me the letter, so I can read it to Jim.

Do you have Reid's number?

PANEL LIAISON BEHRMANN: I do.

CHAIRPERSON ANASTASIO: He didn't leave a folder, did he?

PANEL MEMBER GLANTZ: This is why you can't retire.

(Laughter.)

CHAIRPERSON ANASTASIO: Right. This is a great example of what life is going to be like without Jim.

(Laughter.)

CHAIRPERSON ANASTASIO: And so Panel members after I read the letter, what we'll do is once the meeting is adjourned, we're going to take a picture with Jim. And then we'll get a copy of that picture to Jim as another token of our appreciation of all his service.

PANEL MEMBER GLANTZ: Maybe we should take the picture while we're waiting for Reid.

CHAIRPERSON ANASTASIO: You know, that is an excellent point. Why don't we take our picture now.

(Off record: 1:52 p.m.)

(Thereupon a recess was taken.)

(On record: 2:02 p.m.)

CHAIRPERSON ANASTASIO: All right, everybody. We're back in action. Okay. So our last item of business is this letter from the California Environmental Protection Agency and the Scientific Review Panel to Jim Behrmann in appreciation of all of his -- all the service.

And the letter reads, "We wish to express our gratitude for you exemplary commitment and service to California's Air Toxics Programs, as the California EPA's liaison to the Scientific Review Panel on Toxic Air Contaminants for 19 years.

"The Panel is responsible for the technical peer review of draft health risk assessments of candidate toxic air contaminants, new guidelines for the preparation of improved health risk assessments, summaries of the derivation of health values for other contaminants, and related documents.

"During your tenure, you assisted the Panel in formulating dozens of formal notices and findings, to assure their legal soundness, and that all key points and conclusions were included. You also directed staff in the planning of Panel meetings, which often involved challenging logistics, given the full schedules of Panel members, timely needs to the State, and other factors.

"Your careful attention to the Panel's needs, as well as to the scientific details of the documents under review has enabled the Panel to run smoothly and efficiently, and to issue new findings and conclusions that have led to advanced health protective policies and measures. The end result is that we can all breathe cleaner air today.

"The details of the Scientific Review Panel's work and its contributions are critical to the development of State regulation and policy. Over the years, the Panel listed 21 toxic air contaminants and nine pesticide toxic air contaminants, and reviewed technical support documents

for the Air Toxic Hot Pots Program and the Air Toxics Hot Spots Guidance Manual.

"The Panel's independent careful review of proposed actions, risk assessments, and guidelines assures the public, as well as the regulated businesses, that the scientific underpinning of the agency's regulatory work is sound.

"We thank you, Jim, for your service and your contributions in assisting the Panel in improving the health of all Californians. And we extend our warmest wishes to you for a long and happy retirement".

Sincerely, the Panel.

(Applause.)

PANEL LIAISON BEHRMANN: Thank you.

CHAIRPERSON ANASTASIO: So we'll miss you a lot Jim, but we're very happy for you that you're going to a happy place.

(Laughter.)

CHAIRPERSON ANASTASIO: With that, can I get a motion to adjourn?

PANEL LIAISON BEHRMANN: Is it okay if I --

CHAIRPERSON ANASTASIO: Oh, sorry. The guest of honor would like to -- you have to speak into a mic for the record.

PANEL LIAISON BEHRMANN: I just wanted to express

my personal appreciation to the Panel. This was just an unexpected gift. Thank you very much.

But working with this Panel just has been a nice -- actually a second half to my career here. Having worked throughout the Board starting several decades ago, it just, it was a perfect way to close out my career.

So each of you individually, as well as I have many, many friends working for the Board. It's just a wonderful place to work and for people to be with.

So thank you all very much.

CHAIRPERSON ANASTASIO: That's great. Thanks, Jim. We wish you the best in retirement.

PANEL LIAISON BEHRMANN: I'm still going to be here until end of the year, but on vacation.

(Laughter.)

PANEL LIAISON BEHRMANN: So I will see you -- I will see you in November at the November meeting.

PANEL MEMBER HAMMOND: But that's a call-in meeting.

PANEL LIAISON BEHRMANN: Yes. Yes.

CHAIRPERSON ANASTASIO: He'll talk to us on the 22nd. Yeah.

Okay. With that, can I get a motion to adjourn.

PANEL MEMBER KLEINMAN: So moved.

CHAIRPERSON ANASTASIO: Can I get a second?

PANEL MEMBER GLANTZ: Second

CHAIRPERSON ANASTASIO: Can we take a vote. All in favor

(Hands raised.)

CHAIRPERSON ANASTASIO: It's unanimous. Thank you all for your input on today's meeting. We'll talk to you on November 22nd.

(Thereupon the California Air Resources Board, Scientific Review Panel adjourned at 2:06 p.m.)

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

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 13th day of October, 2019.

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