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STATE OF CALIFORNIA

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

ENVIRONMENTAL CONTAMINANT BIOMONITORING PROGRAM

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Dr. Tina Bahadori, American Chemistry Council

Dr. Dana Barr, Emory University

Dr. Dale Hattis, Clark University

Dr. Amy Kyle, University of California, Berkeley

Ms. Ruthann Rudel, Silent Spring Institute

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Ms. Amy Dunn, Safer Alternative Assessment and Biomonitoring Section

Ms. Fran Kammerer, Staff Counsel

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ALSO PRESENT

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Dr. Asa Bradman, University of California, Berkeley

Dr. Roy Gerona, San Francisco General Hospital

Dr. Ulrike Luderer, University of California, Irvine

Ms. Sharyle Patton, Commonweal

Ms. Susan Ryan

Dr. Gina Solomon, University of California, San Francisco

Ms. Rachel Washburn, Loyola Marymount University

Dr. Mike Wilson, University of California, Berkeley

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PROCEEDINGS

OEHHA ACTING DIRECTOR ALEXEEFF: Good morning, everyone. I'm George Alexeeff, Deputy Director --

(Laughter.)

OEHHA ACTING DIRECTOR ALEXEEFF: Oh, excuse me, Acting Director, sorry, of for the Office of Environmental Health Hazard Assessment, in the California Environmental Protection Agency. I want to welcome the speakers and the Scientific Guidance Panel members, the public, staff, and the audience participating via the webinar to the Biomonitoring California's Workshop, also known as the California Environmental Contaminant Biomonitoring Program. And the workshop is on understanding and interpreting biomonitoring results.

I particularly want to thank the speakers who have traveled from all over the country for coming to discuss this important topic with us.

First, I'll mention a few logistics. Restrooms, out the back door and to the right. And then emergency exits. The nearest exit may be behind you.

(Laughter.)

OEHHA ACTING DIRECTOR ALEXEEFF: And then we have some in front over here too.

So I want you to know this meeting is being transmitted over the Internet as a webinar, and is being

videotaped and transcribed. There will be a transcript of the meeting, and it will be posted on the website in several weeks.

I would like everyone speaking, particularly if there's questions from the audience to wait until there's a microphone available and speak clearly into the microphone.

The reason for holding this workshop is to get input on how we should approach the interpretation of biomonitoring results. One aspect is to help us with explaining results to individuals participants.

The Program also needs to interpret the results at the population level, to help the State evaluate how well its regulatory programs are addressing environmental exposures to contaminants.

So I'd like to introduce Sara Hoover. She's the Chief of the Safer Alternatives Assessment and Biomonitoring Section in OEHHA. And she will talk about the goals of today's workshop and introduce this morning's speaker.

Sara.

MS. HOOVER: Good morning, everyone. Thanks again for joining us. And again, a special thank you to the speakers, because it's been a lot of work over many months for us to put this together, and we really

appreciate your participation.

(Thereupon an overhead presentation was Presented as follows.)

MS. HOOVER: So as George said, we're going to be talking today on understanding and interpreting biomonitoring results.

Let's see, how do I advance this guy.

All right. Lee, arrow?

Oh, I was slow.

So just to go over the workshop objectives, which were in the description of the workshop. We're going to be discussing, in general, approaches for understanding and interpreting biomonitoring results. We also want to specifically start to tackle this issue of comparison levels in blood or urine.

And just to say what I mean by that. In the -- yesterday, if you were at the workshop yesterday, there was a term used called levels of health concern. That would be a type of comparison level. At the last SGP meeting, we were using the term biomonitoring reference levels. So that's what we're alluding to when we talk about comparison levels today.

In terms of more specific issues, we also want to look at particular scientific challenges in interpreting results, including how we should address multiple chemical

exposures and sensitive subpopulations. And we're really eager to get the audience and speakers and the Panel's input onto Biomonitoring California on these issues.

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MS. HOOVER: So just to reiterate some of the background that George was talking about. The context for why we're doing this is two-fold.

One is related to individual participants. We -- under Biomonitoring California, we're mandated to return individual results to participants if they request them. And we are also just, as part of the legislation, but just as part of conducting these projects responsibly, we'd be advising individuals on follow-up steps as needed. So that's the individual level.

Then another goal of the program is to help California to use biomonitoring results to help California evaluate public health efforts to reduce chemical exposures in this State. So that means we're going to be looking at results both at the individual and population level.

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MS. HOOVER: So some of the interpretation issues that could come up is understanding what is an elevated blood or urine level for a particular chemical and deciding on follow-up steps and when to take those

follow-up steps.

Another, if you were here yesterday, you heard a really great talk by Rachel Morello-Frosch and Holly Brown-Williams of UC Berkeley about report-back issues. So some of that is how do we provide context for individual results and answering questions that the participants might have about what their results mean.

We also want to be able to explain what biomonitoring results are and what biomonitoring is in general to the general public. And again, trying to evaluate chemical exposures at the population level to help guide public health actions on chemicals of concern.

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MS. HOOVER: So based on the objectives, we've just tried to layout some general discussion questions, and of course we also welcome other kinds of input. So just we're -- over the day, we're going to be thinking in general about what approaches should be used to understand and interpret biomonitoring results.

We'd also like to hear about what information people think is needed to properly interpret and explain biomonitoring results at the individual level and at the population level.

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MS. HOOVER: And then we do want to talk a little

bit about this issue of comparison levels. So an obvious comparison level is measured levels in other relevant populations. So other than that, what types of comparison levels in blood or urine would be useful for providing context for biomonitoring results, both at the individual level and the population level, and what methods might we consider using to develop these comparison levels.

And then we wanted to bring back these specific questions, in particular, about how should biomonitoring results of multiple chemicals that either act in the same way or produce the same health effect be interpreted at the individual level, and at the population level. And as well as, how should sensitive populations be taken into account at the individual and population level.

So I'm putting these up now so people sort of have them in their mind over the day and then we're going to be talking about them more specifically in the afternoon session.

So just to give you an idea of how the agenda is going to work. We're going to be hearing from 3 speakers in both the morning and the afternoon. And we're going to have time for a few questions right after the speakers give their talk. Then we've also allotted a half hour session in both the morning and the afternoon where we're going to have the 3 speakers come up, maybe comment on

each other's talks and take additional questions and discussion from the audience. And then in the afternoon, we're going to have a panel discussion with all 6 speakers interacting with the audience and going over some of these questions.

So I'd like to start just by introducing our morning speakers.

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MS. HOOVER: So we're really pleased to have Dr. Dana Boyd Barr here. She's a professor of Exposure Science in Environmental Health at Emory University. Before joining Emory, she was at CDC for 22 years, and she spent much of her time developing methods for assessing human exposure to a variety of environmental toxicants. And she serves on many national and international panels and committees related to exposure assessment.

Her current research includes studying maternal and child health, paternal reproductive health and farmworker safety in Thailand. She's also collaborating on several child and farmworker cohort studies in the U.S. in evaluating brominated flame retardant exposures and thyroid function in small children.

Our second speaker this morning is Ruthann Rudel from Silent Spring. She's a research director at Silent Spring Institute, where she leads exposure and toxicology

research on endocrine disrupting chemicals and on mechanisms by which chemicals may influence breast cancer risk.

She's also an Adjunct Research Associate in the Brown University Department of Pathology and Laboratory Medicine, and serves on the NTP Board of Scientific Counselors.

She directs the Silent Spring Institute's Household Exposure Study, which collects data on indoor and outdoor air, house dust, urine, blood and self-reported exposures. And there's participants in California and Massachusetts in those projects.

And Silent Spring works on developing ethical and effective methods for reporting personal exposures to study participants when the health implications are uncertain.

And then our third speaker this morning is Dr. Tina Bahadori. She's managing director for the Long Range Research Initiative Program at the American Chemistry Council, which is a research program designed to support chemical management decision making.

Before she joined ACC, she was manager of the Air Quality Health Integrated Programs at the Electric Power Research Institute. And she also serves as a member of a number of boards and committees, such as the National

Academies' Board on Environmental Studies and Toxicology, the Board of Scientific Counselors of CDC, the Chemical Exposure Working Group on the National Children's Study, and she's also been involved with the CDC National Conversation on Public Health and Chemical Exposure.

So welcome to the 3 morning speakers. And I'd like to ask Dana to come up and start her talk.

(Thereupon an overhead presentation was Presented as follows.)

DR. BARR: Good morning. First of all, I'd like to thank Sara and Lauren and all the other people who are responsible for conducting this workshop. I think since the National Academies of Science had their work group on biomonitoring come out with a report in 2006 indicating that we were very good at producing a lot of biomonitoring data, but very poor at interpreting the biomonitoring data. That we kind of outpaced ourselves. That it's really good to see California being so progressive in taking on this issue, which I would say is timely, but I actually think it's more needed long ago. And so I'm glad that we've had the opportunity to get together today to discuss this.

I'm also happy that I can be the first speaker. First of all, I get to go back to a lot of the basics. But as a self-proclaimed queen of biomonitoring, it's my

pleasure to able to talk to you about some of the things that we've done in the past that we know worked really well, some of the things that didn't work as well and where we can move into the future

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DR. BARR: So back to the basics. This is a typical source effect diagram. It's kind of a permutation of one that EPA uses that shows that an environmental chemical can actually -- I'm going to use the mouse here to get to the -- to use it as a pointer, but can get into environmental media.

And we can measure a chemical in that environmental media. That becomes the external dose. The internal dose is after that chemical or agent is absorbed into the body. We can measure that in a biological tissue, an excrement, or in a distribution matrix. And, of course, the net environmental chemical may go on to produce some effect.

I do want to point out that a biomonitoring measurement is not equivalent to exposure. It's an assessment of exposure. Exposure really is the occurrence of that chemical at the interface between the environment and the human. I also want to point out that body burden is not necessarily a biomonitoring measurement. It's somehow a cross section between what's in our blood,

what's in our distribution matrices, et cetera.

And so in order to avoid the exposure conundrum, where we're not speaking the same language, I want to define a few terms, because it's very hard to agree on interpretation of complicated issues when we have incongruent view of what exposure is or what specific terms are.

And so the first term is exposure. The contact of the chemical or agent at the biological interface.

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DR. BARR: Body burden, the amount of the chemical agent residing in the body, including the deposition matrices

And biomonitoring then would be a measurement of that chemical, its metabolite or reaction product in a biomatrix, most commonly blood and urine, but can be any biomatrix.

Body burden then does not necessarily equate to a biomonitoring measurement. And the biomonitoring measurement does not necessarily equate to exposure. So I just want to make sure that we're talking about the same things here.

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DR. BARR: So why are we biomonitoring?

Well, we're biomonitoring for a variety of

reasons: To assess exposure, to see what chemicals actually get into people, to assess the effectiveness of regulatory actions, to evaluate interventions. There are a lot of reasons. But the bottom line is we want to understand if environmental exposures have anything to do with disease.

And if they do have anything to do with disease, what can we do to prevent those exposures, so we can reduce the disease outcome. So that's kind of it in a nutshell.

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DR. BARR: But biomonitoring data are not created equally. There are a variety of factors that can affect both the quality of the biomonitoring data that go -- range from study design to sample direction to sample analysis and even how we treat the data afterwards.

And so these are some of the issues that I'm going to talk about, because these are some of the complexities that you encounter when you try to interpret biomonitoring data.

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DR. BARR: First of all, biomonitoring data hinges on the inherent characteristics of the exposure scenario. And I'm using the word "hinge" here knowing that it actually relates to one factor, but I'm taking

some literary license here, because I think it needs to be emphasized a little bit more than just saying it depends on.

We know that high levels of exposure are not equal to low levels of exposure. And we can't necessarily extrapolate high level of -- high exposure levels or high exposure effects to low levels and low effects.

And I think lead is a pretty good example of that. When we saw that lead was in use in gasoline, people had high levels of lead in their blood. Because we used some interesting data from high level exposures to try and interpret or try to predict what people would have in their blood after the removal of lead from gasoline, we were wrong. And I think that that's a good example of how you can't necessarily translate high level exposures to low level exposures.

Also, the chemical or agent that one is exposed to or that may be measured may differ depending upon the exposure scenario. An example would be urinary benzene. The chemist in me says that benzene is never going to end up in urine. It just is not going to happen. It's too lipophilic.

But I think current data have shown that when you have high enough levels, especially in occupational settings, that urinary benzene becomes one of your most

selective markers for evaluating benzene exposure in occupational setting.

Another example is the herbicide atrazine, which is second most abundantly applied herbicide or pesticide, in fact, in the U.S. And the structure is shown here. And it's applied primarily to corn and to turf applications.

When people are applying these occupationally, they're exposed to atrazine and degradates and contaminants of atrazine. So their exposure profile may look very different than if you get an environmental exposure where that chemical has been weathered in the environment. Some of the alkyl groups have been removed. The chemicals don't look the same. Although, they're still biologically active.

And so again the exposure scenario may dictate what you need to biomonitor.

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DR. BARR: Biomonitoring hinges on the study design too. Exposure is dynamic. It doesn't occur once at the same level always at the same time for most chemicals. And I have this drawing here, the New Game of Human Life by John Wallis, which was a precursor to Milton Bradley's Game of Life.

But if any of you have ever played the game, you

know that each decision you make at each point in time will dictate what happens to you during that game. And that's what happens with exposure too. So if you're exposed in utero, it might dictate what happens to you when you're 2 years old or even when you become an adult.

And so exposure is dynamic and it changes over time, so it's not constant and it's -- not necessarily constant. So therefore predicting exposure becomes difficult unless you have repeated empirical data. And I think that that's a very important concept, that cross-sectional data are nice, but repeated empirical data are necessary.

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DR. BARR: Biomonitoring hinges on the preanalytic characteristics. And I know that there are probably a lot of chemists in the room, which is rare when I give a presentation, so I'll talk about sample collection.

Were the samples collected properly? Was contamination properly avoided? Were they stored properly? And I do want to point out that these are things that really affect your interpretation of the biomonitoring results, but sometimes these variables are just luxuries.

If you're in the middle of an emergency response,

for example, you take whatever kind of samples you can get. And you may not be able to account for all of the storage and the sample contamination and such issues. And so, sometimes you have to consider this in a post-hoc evaluation of the data.

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DR. BARR: Biomonitoring hinges on the analytical measurement. All numbers are not created equally. I think we all know this. There are various analytic techniques. I think the ones that are primarily promoted in biomonitoring today are mass spectrometry based, but they are not the only analytic techniques that provide quality data. We have immunoassays and a variety of other techniques that can be used.

You need credible validation of these biomonitoring methods. And By credible validation, I mean validation that makes sense. You need to look at the analytical precision. You need to look at the accuracy. You need to understand that some of these parameters are dynamic as well. You can characterize the parameters of a method, but they change over time depending upon analysts, the age of the instrument, other factors. So you can't just calculate it once and think that it stays the same.

The same is true of a limit of detection. A limit of detection is not static, but is dynamic, and can

change from sample to sample. So if you want to do a statistical measurement over a 60-day period of time to really solidly get down that limit of detection, it's only going to be 60 days wasted, because you're going to have to recalculate it again for the next study.

Analytical. We need the analytical ability to differentiate between 2 similar chemicals. And we need to understand the method characteristics and measured values are not static, but they do -- they can change with time, depending upon the analytical methodology, the age of the instrument, the analyst, and such.

And I think then in recognizing that, quality data has to include this recognition that data are limited. The numbers are not solid, in that they aren't changing over time. They have limitations too. And I think we, as people that are interpreting data, want to take these numbers and act like they have no uncertainty associated with them. And I think that we need to recognize that. And failure to recognize that means I think a failure of quality.

I think inter-laboratory comparisons are needed, not single laboratory qualifications. The reason for that is if one laboratory is used as a reference laboratory, if that has a bias with it, then the whole system is biased. There are several inter-laboratory comparison programs out

there, like the German EQUAS program. And even for clinical reference values where they enlist multiple laboratories to try and define that reference value. And so they can ensure that there's not one laboratory bias that's driving the whole force.

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DR. BARR: So biomarker hinges on biomarker specificity. And I have several slides about specificity, and it has to do with the specificity of the analysis and the specificity for the chemical too which one is exposed.

So is the biomarker selected for the chemical agent it represents?

Well, again, this likely differs based upon the exposure scenario. And here I give the example of 1-Naphthol as a biomarker of exposure to either carbaryl, which is a carbamate insecticide, or naphthalene, which is low molecular weight PAH.

If you are in the environment, one would assume that predominantly you're being exposed to naphthalene not carbaryl. So most of the 1-Naphthol in your urine is going to be from exposure to the PAH and not exposure to carbaryl.

However, if you're a carbaryl farmer, and you -- and we encountered one of this in the pilot agricultural health study -- and you go and apply carbaryl in your farm

and you come back covered in carbaryl, most of the 1-Naphthol in your body is going to be from carbaryl. So again, the exposure scenario comes into play when you're trying to interpret the data.

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DR. BARR: The chlorpyrifos story. I have to look up at Asa when I see this, because we've learned a lot about chlorpyrifos exposure and assessing chlorpyrifos exposure over the last decade. And I think it's moved us very much forward from where we were 30 years ago.

One can be exposed to chlorpyrifos, which is an organophosphorus insecticide, or its environmental degradates in the environment. And its environmental degradates include the oxon, which is the active metabolite or the hydrolytic products, which are right here below.

They hydrolytic products are not toxic. The oxon is toxic. Chlorpyrifos is toxic. So if you measure the bottom chemicals that are excreted in urine, you have exposure to consider from chlorpyrifos, its oxon, and its nontoxic environmental degradates as well. And so that confounds your interpretation of that exposure.

If you measure just chlorpyrifos in blood, which is probably the most selective measure, it's a great measurement to make, but it's a very complicated

measurement to make. The levels of chlorpyrifos in blood are usually along the order of 3 orders of magnitude lower than urinary metabolite levels. And that measurement is subject to a lot more error and is more costly.

So you have a lot of things that you have to consider and weigh for in order to interpret the data that you're generating. And I think we're understanding a lot more now about chlorpyrifos exposure and what we know and what we don't know.

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DR. BARR: So again looking at the specificity, is the matrix appropriate. Why don't we measure PAHs in blood?

Well, one of the reasons is because PAHs are everywhere, and it's hard to account for contamination in blood. So urinary benzene I already talked about. No one that's a chemist would -- or even maybe a toxicologist would think that benzene itself would end up in urine, but it does.

Well, what about urinary benzo[a]pyrene?

Well, it's not representative of benzo[a]pyrene exposure, because most of the hydroxylated benzo[a]pyrene metablites are excreted in the feces. Conversely, the chemically similar pyrene is predominantly -- its hydroxylated metabolites are predominantly excreted in the

urine.

We also look at other matrices, like saliva. And here I show salivary cotinine and serum cotinine. And there's roughly a 1-to-1 correlation. So this indicates this might be a very good matrix for biomonitoring. But if we do that, we have to ensure that we're not getting contamination from breathing in tobacco smoke or from active tobacco -- from actively smoking tobacco as well. So there's some issues there that need to be considered.

Also, I'm going to talk in a minute about nPOPs and POPs, it's Persistent Organic Pollutants and Non-Persistent Organic Pollutants. And one of the things I want to challenge you with is whether or not we should be measuring nPOPs and lipid-rich matrices. And I'll talk about that in just a moment.

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DR. BARR: So biomonitoring hinges on biologic variability, coexposures and comorbidity. And I'm not going to get into this a whole lot, because Tina Bahadori is going to be talking about this concept, which is called the exposome in a moment. But if you're looking at pollution-related exposures and you're looking at blood concentrations, they're usually in femtomolar to nanomolar range.

But if you look at dietary and endogenous

exposures that result from stressors, it could lipid peroxidation products, reactive oxygen species, quinones, They're usually about 3 orders to 6 orders of magnitude higher than the environmental chemicals in people. So I think is something we can't ignore, because it certainly is going to play some sort of a synergistic, or, if not synergistic, at least some role in how our body handles the insults from environmental exposures.

And the exposure to exogenous and endogenous chemicals can vary, anywhere from 10- to 1000-fold within and among people. And so this variability again is another issue that we have to address and why I think that repeated measures is going to be required.

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DR. BARR: Chemicals in a single class also may have different metabolism and bioaccumulation characteristics. And I talked about PAHs and how benzo[a]pyrene and pyrene could be eliminated differently. Phthalates would be another example that I'll talk about. But even things that we think we have a great handle on, like PCBs that we've been measuring for 30, 40, 50 years, even those we understand that they behave differently now, that some of them behave differently than others.

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DR. BARR: This is an example with phthalate

metabolism. This is a dimethyl substituted phthalate. And normally what you have is a normal hydrolytic process occurs, you lose one of the alkyl chains and that's excreted as its phase 2 metabolite in urine, and that can be measured. That's called the monohydrolytic product or the monoethyl product.

And for this particular example, I'm going to use diethyl -- diethyl-2-hexyl phthalate. When we measured diethyl -- mono-ethylhexyl phthalate, we only see about 150 parts per billion as a median value in the U.S. population -- or as the 95th percentile in U.S. population.

However, because this is a large molecular weight phthalate, it undergoes further oxidation and elimination, which produces multiple chemicals then that are excreted in the urine. And if we don't consider those, we can underestimate exposure.

But now here we have 2 issues. If the mono-ethylhexyl phthalate is considered the biologically active component, and the oxidative metabolites aren't, are they interesting chemicals to measure?

Well, it depends on whether you're trying to evaluate exposure or you're trying to evaluate health. Again, it goes back to the exposure question, and perhaps the exposure scenario.

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DR. BARR: I think that biological persistence is a key factor for consideration in interpreting data. And most of you have seen some version of this graph throughout your career, but I've kind of tried to simplify it a little bit, with these red lines being blood levels and the dotted line down here and the red line up here representing what we would expect in blood and urine after exposure to a persistent organic pollutant. The exposure occurs here at the Y axis.

And for a persistent organic pollutant, we usually have this slight decline here, which is a called an alpha distribution, which represents that chemical being equilibrated among the distribution matrices. And then we have a fairly slow decline of this chemical in the blood. So we can take a blood sample, measure it, and kind of indicate whether that person has had exposure to Persistent Organic Pollutants.

Conversely, if they're exposed to a non-Persistent Organic Pollutant that's really typically short lived in the body, we have a similar occurrence, an increase in the blood levels. We have a more dramatically sloped alpha distribution. But I think this is important and something we tend to ignore, that that alpha distribution does represent distribution among the various

matrices.

And then we have a decline in the blood levels and a concomitant increase in urinary metabolite levels, why is most of the non-Persistent Organic Pollutants are measured in urine, because we have a longer window of exposure to capture -- or a longer window to capture or assess that exposure. It's an easier measurement, because the chemical concentrations are higher, and sometimes the measurement -- though sometimes the measurement is not as meaningful as the blood measurement.

And typically, the Persistent Organic Pollutants again are measured in blood, because there's very little appreciable elimination of Persistent Organic Pollutants in urine.

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DR. BARR: But now for the curve ball. Not all Persistent Organic Pollutants biologically persist. And not all non-Persistent Organic Pollutants fail to bioaccumulate.

And so this varies not only among person, but also within persons. And here I'm showing some data that we published back in 2006 with Philippe Grandjean as apart of his Faroe cohort study, looking at low molecular weight PCBs and a representative high molecular weight PCBs. So this is PCB 28 and this is PCB 153.

And what we found is that people that were exposed through breast feeding or continued eating Of blubber had variable levels of PCB 28. PCB 28 has a very short biological half-life compared to other PCBs. But we still lump it into this Persistent Organic Pollutant category.

PCB 153, however, which is a very -- this is the most prevalent PCB congener, was highly associated with breast feeding, even at 14 years of age and with blubber consumption.

And so I think that we start thinking of these concepts of POPs and nPOPs as being one way, and we can't grasp changes that we find out about these particular chemicals over time. And we've known this for over five years.

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DR. BARR: So chronic exposure is really a different story. We have repeated exposures, and so a single measurement makes it a lot easier to interpret. An example, environmental tobacco smoke, perhaps lead or some other chemicals.

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DR. BARR: Then we have issues of whether or not if to creatinine adjust or lipid adjust these chemicals. Is creatinine adjustment of urinary concentrations

appropriate?

Well, when you look at a distribution in the population here, you see children have about half the level of creatinine as normal adults do. And so if you creatinine adjust, you're artifactually increasing that child's level by 2. I think it's kind of interesting that we've tried to put forth methods to avoid artifactually making this change. But even if you look at CDC's report, and the values that -- the least squared geometric means where they've corrected for creatinine, most of the urinary metabolites they say are about twice as high as adults, but you don't see that same thing in blood. And it just seems to not make sense and not add up. And I think it really needs to be evaluated more stringently.

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DR. BARR: And this maybe is an indication that we should strive to collect more integrated samples anyway, so we don't have to worry about these correction processes.

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DR. BARR: We have to evaluate biomonitoring data on a population level. But of course people want to know their exposures, so how can we provide a contextual framework given our current knowledge?

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DR. BARR: I think that we obviously can give them positions in overall distribution. Reference ranges have reasons for our -- or are useful for being able to compare different concentrations to. But I also think we need to provide some context to relate to common exposures and biological measures.

For example, caffeine, or acetaminophen, or aspirin. Here, I show a distribution of caffeine in a selected population. And the units are about 3 orders of magnitude higher than most environmental toxicant levels. And so I think this helps to put it into some perspective.

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DR. BARR: So biomonitoring hinges on our ability to meaningfully interpret data with respect to exposure disease. This often requires some timing of exposure, pharmacokinetic information. It may require uptake information and certainly requires a lot of studies.

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DR. BARR: So now that I've told you a lot of the complexities of biomonitoring, I mean, does it really answer any questions?

Well, I've put certain questions down here in the left-hand side of this column. For example, temporal trends in exposure, risk, exposure itself, risk mitigation, and whether cross-sectional biomarker data

answer those questions, longitudinal data or environmental data, and maybe what are some of the data gaps.

I think that what I find is that, yes, biomonitoring data are useful in helping to answer some of the questions, but they're not all we need. We can't use biomonitoring data in isolation to try and get at the exposure and disease-related questions that we want.

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DR. BARR: And, of course, none of us want to deal with the unexplored territory mixtures, even though continuing to avoid addressing them doesn't mean that they'll disappear. And I hope that Tina Bahadori will talk a little bit more about how we can address mixtures later.

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DR. BARR: So I think that we've had many successes and pitfalls for biomonitoring. We've come along way. We understand now more than ever a lot of the issues that are related to it. We also have a better understanding of what we don't know. And we have some successes under our belts.

But I think that if we continue in the direction that we are going now, where we're just very narrowly focusing our efforts, it can be our demise, because we really need to do a lot more to understand if there's a

relation between exposure and disease.

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DR. BARR: So I would suggest an unconventional approach. And that biomonitoring in isolation is just not sufficient. Coexposures and comorbidity should be addressed. And then we should advocate studies with holistic approaches to exposure science. And this can include non-hypothesis driven exploration, but also it needs to be linked back to some toxicological relevance.

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DR. BARR: I think it's important that several of our leaders in science have acknowledged the need to produce both genomic, epigenomic and exposure data combined in order to be able to interpret the relation between disease and exposure.

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DR. BARR: For example, Linda Birmbaum recently said, "This is the decade of the epigenome". And we need genomics, epigenomics, and environmental exposure data in order to understand these complexities.

And Paul Anastas, the Assistant Director for EPA and the Director for ORD said this is going to represent a seismic shift for the Agency to stop thinking about exposures on a chemical by chemical, toxicant by toxicant, even matrix bay matrix basis.

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DR. BARR: So now we have a new dilemma. Do we continue to biomonitor and do things the way we used to or do we think outside the box and do things a little bit differently, so we can try and really get at some of those questions that are -- that need to be answered in order to see if we can link exposure to disease?

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DR. BARR: And so I would like to say a quote that one of my dear friends, Matti Jantunene at his retirement seminar at the ISES meeting said, and that's, "Life is a consequence of and adaptation to the exposome", where the exposome is a collection of exposures over a lifetime that we need to evaluate.

And here, it's of importance to me. This shows my daughter in my womb. This shows her the day that she was born. And I do believe I had a conference call with Asa Bradman and Brenda Eskenazi on that very day about the CHAMACOS cohort.

(Laughter.)

DR. BARR: It shows a variety of stressors she's had throughout her life and some of the exposures. And I think that we need to take -- look at all of these collectively when we're looking at interpreting biomonitoring data, in order to make our children's

ability to adapt to these exposures much more feasible.

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DR. BARR: Lastly, I'd like to just maybe give this in loving memory of Larry Needham, who was my long-time mentor, a biomonitoring guru, and somebody who thought outside of the box, even though his bread and butter was in the box. And he was a beloved mentor and friend for over 25 years and he's greatly missed by many, including many in this room.

And thank you for your time and your attention.

(Applause.)

MS. HOOVER: So we do have a few -- well, actually more than a few. We have the full time for questions, because Dana got through her talk very well. So if anybody has questions, we have a mike going around. Any questions for Dana?

Oh, before you ask your question, can you please identify yourself.

DR. BAHADORI: Tina Bahadori, American Chemistry Council.

Great talk, Dana.

So what do we do now?

DR. BARR: Well, I think that we've seen a lot of talks and a lot of information over the last year on exposomics, where we actually marry this top-down

approach, where we look at perturbations in various systems that are caused by multiple exposures, multiple stressors. And then we anchor that with a bottom-up approach looking at chemicals that we know can be present, that we know can potentially cause disease.

And so we try and look at the body holistically. That recreates one system then, one disease, one system that needs to be incorporated using probably systems biology approaches into a more complex system. And I think that -- I think this is an area where we are just starting to break ground, but I think it's where we're going to find the most information that's going to enable us to not only understand the environmental component to disease, but also the genetic component, because I think that they work collectively.

DR. HATTIS: I think also wonderful -- Dale Hattis, Clark University.

A wonderful talk. And I think a couple of your points deserves emphasis. And that is the tradition in biomonitoring of going for the largest possible N by making one measurement per person can be counterproductive. That, in fact, you have -- you can get much more information if you have more measurements per person. Although, that imposes burdens on both the researchers and the subjects. But also making the

measurements themselves is only the starting point for what can be a considerable enterprise at creative analysis and interpretation that may often be, I think, neglected in favor of building your N.

DR. BARR: Thank you, Dale. I appreciate that. I think now we also have an opportunity to leverage on a lot of studies that are out there. I mean, for example, the National Children's Study collecting a lot of samples. I mean, if we're very creative, we can come up with some really interesting ways to look at disease as apart of that population.

I also want to advocate -- and I know Asa I've called you out 3 times already today -- but advocate Asa and the groups at Columbia, Berkeley, Cincinnati, Mount Sinai, who are taking this approach where they have these great cohorts that are very data rich, and they're combining the data to get more meaningful results out of it. And I think that we should encourage people to do more like that. We, as academicians and as researchers, tend to kind of hold our data close to us, because we want to maximize what we can get out of it.

But I think that by taking on those approaches that we're leveraging existing data and trying to make more sense out of what we have as well.

DR. ZEISE: Thanks. A wonderful talk. I was --

MS. HOOVER: Identify yourself.
DR. ZEISE: Pardon?
MS. HOOVER: Identify.
DR. ZEISE: Oh, Lauren Zeise, OEHHA. I was wondering if you could comment a little more on the relationships that lead to uncertainty in your actual measured value, and indicate how you might get a handle or if you have a handle on the magnitude of those and how we might find out about that?
DR. BARR: Yeah, I mean, obviously when you develop a method -- and I know that there was a lot of talk yesterday about validating the methods. And that's what you do. You find out about the uncertainty, about the accuracy that's involved with it.
But as I mentioned, that's not a value that stays the same. That value changes over time, as does the LOD. And so what I think you have to do is reevaluate this on a constant basis. Now, typically you're in the same ballpark, the same order of magnitude. But, you know, for example for some studies that we'd done, the LOD might be a factor of 10 higher, because our equipment is 10 years older, and our analyst is brand new.
And so those kind of factors can play a role in it. So I think that I would advocate for each individual study having all of those characteristics evaluated, the

LOD, the accuracy, the precision. So for an individual set of data, then you'll have all of that information.

DR. ZEISE: And does CDC now report that? I realize they report the LOD, but it's the precision and the accuracy measurements.

DR. BARR: They report the published analytical methods. To my knowledge, they don't report it with each individual data set.

DR. ZEISE: Thank you.

MS. HOOVER: Thank you.

DR. BARR: Thank you.

MS. HOOVER: Thanks, Dana.

And next we're going to hear from Ruthann Rudel from Silent Spring.

(Thereupon an overhead presentation was Presented as follows.)

MS. RUDEL: Hello. Good morning.

And thanks for inviting me to be here in the context of your thinking about how to report back to participants and to the general public in the context of the California Biomonitoring Program.

I am happy to be here and share, I think, just a few thoughts derived from -- about our experience measuring personal exposures, reporting back to people, and then also interviewing people after they got their

information to try to understand what meaning they took from that.

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MS. RUDEL: For those of you who aren't familiar with Silent Spring institute, I'll just quickly say that it's a nonprofit scientific research organization. It was founded in the mid-1990s by breast cancer activists to do research specifically on environmental factors that might be related to breast cancer.

We have a scientific staff. We collaborate often with academic investigators. We're funded primarily by government grants as well, and contracts, private foundation grants, and charitable donations.

And I have to -- I should thank Dana and Larry Needham actually, because in our very, very early days before anyone certainly had ever heard of us or had any reason to believe that we would produce anything, they said yes they would do measurements in urine samples collected in our study. So thank you.

So I'm going to -- kind of overlaying everything, I'm going to talk about is really this idea of how to communicate about uncertain science or science.

And I'm going to briefly just review what we've done, and so the experience on which these thoughts are derived. And then I'm going to talk about research ethics

and moving our thinking beyond possible harms, and encouraging thinking about benefits to the individuals in the community associated with the understanding and learning about science, even if it's uncertain.

I'm going to talk about what we kind of boil down to basically 6 questions that people want answers to when we gave them their results. And so I'm going to talk about those 6 questions and how we tried to answer them.

I'm going to talk about this kind of hard job of matching the messages to the amount evidence and the type of evidence that you have, which varies, of course, across compounds and situations. And the idea is that you want to find a balance between avoiding unnecessary worry, but also avoiding false reassurance. And so that's the challenge.

Then I'm very excited actually by this new simple-ish idea. And I think it's responsive also to what some of what Dana brought up at the end of her presentation. And that is that I think one of the opportunities that the biomonitoring programs offer is to follow up on high exposed individuals. And that I think that doing that is going to help us to identify key exposure sources to discover -- essentially to be able to better look for health effects and early effect markers, and to target public health interventions where they're

actually most relevant and needed.

So those are my -- that's where I'm going today.

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MS. RUDEL: So starting briefly with just what we've done at Silent Spring and with our many collaborators, who I will talk about.

So we've done household exposure studies. We've worked in 170 homes. We started at 120 homes on Cape Cod. We've done another 40 homes in Richmond, California here next to the Chevron refinery. And we did 10 homes in Bolinas as well.

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MS. RUDEL: We looked, in general, for about 150 different compounds about almost 90 of them identified in some way as having some kind of endocrine activity. We collected indoor air, in some cases outdoor air, house dust, urine, and results are in these 3 pubs, which you can get on our website.

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MS. RUDEL: And we reported back to people. So I'm going to come back to this -- I'm going to come back to this graph several times. So when we do the report back, we use this basic graph or some variant of it. And it shows individuals what their result was and it shows all of the other homes in the study, as comparison values.

It shows a health guideline, if there was one. And I'm going to talk about those later.

And it tells a little bit about the chemical, where you might find it. So that's the basic format that we use for our reporting back.

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MS. RUDEL: And then our collaborators in the Sociology Department at Brown University went back to people after they had received their results and did interviews about how people made meaning out of the information and what their experience was like.

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MS. RUDEL: This work represents the sustained effort over 10 years by many, many people. At Silent Spring, Julia Brody and I and many of our other staff have worked, you know, extensively on this. Phil Brown in the Sociology Department at Brown University has been involved, especially in report back evaluation of the -- and Rachel Morello-Frosch, who you all -- many of you know at Berkeley and gave a talk yesterday.

We partnered here in the Bay Area with Communities for a Better Environment as we did the study in Richmond. And we have both environmental engineers -- Jack Spengler at Harvard School of Public Health and ethicists and lawyers at the Harvard Law School who have

been all part of our team thinking about this.

And the work's been funded primarily by the Mass Department of Public, by NIEHS, by the National Science Foundation, and by -- you know, whatever else we can raise standing on the street corner.

(Laughter.)

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MS. RUDEL: So the first area is talking about human research ethics and trying to encourage consideration of benefits as well as potential harms. So with uncertain science, we have to ask, of course, what, if anything, researchers should tell the participants about their own results. And we worry could reporting the individual results do more harm than good?

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MS. RUDEL: CDC, on the first page of the NHANES report, addresses these issues specifically and explains that exposure is not the same as disease. That we don't know what level of exposure is associated with health effects for many of these chemicals, and that that research has to be done separately outside of this -- you know, outside of the -- the answers are not in here for that.

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MS. RUDEL: So why should we talk about science

that's just kind of still in progress?

Responsible communication is part of the ethical responsibility in human subjects research. And that in addition to minimizing harm, you're also suppose to maximize benefit and support participant autonomy and justice. And that's the -- if you -- you know, if look at the common rule or how the human subjects research are evaluated, those are the dimensions. And so thinking about possible harm, there's emotional distress and worry. There's a risk of infringing on individual privacy, provide stigma to a community based on findings from these studies, especially -- and again, you know, the uncertainty of the significance makes it harder to consider taking these risks.

There's a potential expense of -- and legal effect of potential ineffective actions that people might take, thinking that -- worrying that there's a risk when there isn't a risk and the, you know, might -- so those are some of the possible harms.

Possible benefits include informed action that is we learn how we can reduce something, and this allows us to make a choice. It's actually increasing environmental health literacy. So we have seen this ourselves in getting into the communities that, as we -- when scientists and public health officials go through the

process of reporting back in a community, it's -- it improves -- everybody learns.

And so the researchers actually get some opportunities for discovery about sources, or other health effects and other -- and the community or individuals gain some knowledge and environmental literacy and occasionally validate some health concerns.

Improves autonomy. For example, it allows people to act in a way that's consistent with their own values. So not everybody is going to be worrying or taking action about a small risk, but some people will want that opportunity. So it does support autonomy.

And the dimension of justice is that if you don't -- if you have the information, you have the power. And if you don't have it, you don't have that -- the opportunities to do that.

And so we've seen building -- also building of community capacity to understand -- to use the data, to take action, to the community co-owns the data and that again is -- is providing -- is increasing their power.

So those are some of the dimensions and ways to think about the benefits and potential benefits of sharing results.

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MS. RUDEL: All right. The 6 questions. It's so

funny, because I always thought it was 5 questions last night. And then I looked at my slide and I counted, and I said there's actually 6 on there. So it's 6 questions.

(Laughter.)

MS. RUDEL: So these are the questions that we felt that people most wanted the answers to. What did you find? How much? Is it high? Is it safe? Where did it come from? And what should I do?

As researchers we're pretty comfortable with the first 2, and the rest get much harder.

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MS. RUDEL: So I'm talking about how we -- so our graph is intended to answer some of those questions. So this is telling the person what the chemical was and how much. Is it high? We can tell them in relation to other comparison, like this study. We can also include other studies, like NHANES or other studies of the same compound in different communities, or different groups.

Is it safe? So the EPA guideline is something that, you know, that we used as a reference level. This is for house dust, we used residential soil screening values. And I'm going to come back to this actually in this point specifically later on in the slide.

But that's what we had access to and felt that we could use, though we had a lot of mixed feelings about

using it for reasons I'm going to explain.

And then where did it come from and what can I do, are somewhat answered by providing information about what the chemical is in and -- so that's how we basically tried to be responsive.

Now, when we first showed these graphs, we said we're going to use these kind of graphs. You know, and other researchers said absolutely not. You cannot give graphs like that to, you know, laypeople. They can't read graphs.

And I should say that there really -- they're pictures. They don't rely on literacy or numeracy to interpret. And, in fact, they've been very effective. And now they've been actually kind of adopted after some testing and focus groups and selected in several of the girl's puberty studies, that are part of the Breast Cancer and Environment Research Centers.

And Rachel Morello-Frosch, I think, yesterday presented work. So they're being improved by usability testing by the Berkeley -- I can't remember that group's name sorry, but...

But the basic idea has so far been actually fairly successful in the field.

Then in response actually to, you know, feedback we got from doing the post -- the interviews after people

got results just from the graphs, is that people also wanted -- some people, anyway, wanted a short text summary of like their personalized headlines, what should I pay attention to in all this hundred chemicals, 3 media, you know, and all this data? What should I pay attention to?

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MS. RUDEL: And so we developed these. And the kind of language that we had in here is just -- these are a few excerpts. Like, "We detected many chemicals in every home in the study". You know, "One of the chemicals we found in your urine is a weed killer..." "If you're using a weed killer in your yard, you could reduce your exposure by controlling weeds without these chemicals". "We are studying this chemical...", because it's endocrine active or this or that, whatever.

And developing these was hard. This is a high level task. It is not amenable to automation. And it requires thinking about this individual's results in -- you know, taken together, and also integrating that into all the other information that a kind of experienced environmental health scientist toxicologist, whatever, you know, risk assessor has, like this chemical is bad, this chemical is good, this health based guideline is wrong, this -- you know, whatever. There's all kinds of information out there that kind of comes into play and

saying, well, I think out of all this information, the most important things are these five.

So that was a challenge, but I think people ask for that. And I think they like that.

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MS. RUDEL: So I mentioned that these post report-back interviews that were done, you know, not just by us calling back our own participants, but by having sociologists trained grad students, and post-docs working to do the interviews. And we interviewed 57 participants who had received their results, 60 to 90 minute in-person interviews that were all transcribed and coded.

And with looking at the basic questions of how do people assign meaning to their results, and what was their experience. And there were 4 papers really reporting on this. JHSB is Journal of Health and Social Behavior, which is not -- we don't know that journal usually. So that's why I'm calling it out.

(Laughter.)

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MS. RUDEL: And so key understandings. So people understood that many chemicals are detected in homes. They understood that banned substances, even if they've been banned for many years, are still found today. For example, we found DDT in two-thirds of the house dust

samples.

They understood that there are many sources for these chemicals. They understood comparisons to distributions of exposure levels in the study -- other people's exposures, and also comparisons to EPA guidelines. And they took understanding that common household or commercial chemicals are unregulated and understudied.

Some quotes -- a couple quotes from these, you know, just to kind of illustrate the kind of reaction or the ways people were talking about it. "I didn't even know there were that many chemicals, but I guess there's a lot more than that even". You know, or, "I'm surprised that they can find many things by looking at your dust and looking at your air. I mean, it's amazing to me that they can actually find chemicals in your air at any amount whatsoever".

So those are just some -- the types of things, and the kind of experiences. Participants wanted their results. We ask -- our autonomy starts with the informed consent. And we say would you like to receive your results?

And, you know, 116 out of 120 Cape Cod people said they wanted to receive their results. And we had a similar, you know, kind of ratio in the California group.

The process really increased the trust in the researchers, between the study community and the researchers. People took pride in contributing to science and contributing to their communities. They expressed frustration at information gaps, where, you know, the question, is it safe? And people really do -- they want the answer to that question. And sometimes we're in a position of saying, well, like, well, we don't know and actually nobody knows. You know, it's not like you can call somebody else.

And they experienced kind of evolving interpretations and brainstorming. So one person originally had said, "Oh, no, we don't use any pesticides in the house". And then we found a fair amount. And we were back there -- we were doing some retesting, I think. So -- because they had some high levels of chlordane, but there were other pesticides there.

And then they were like, "Oh, well, we did have that dog and it had fleas and we bombed the house 5 times, and this and that". So people start to change the way think about it. I went back to their survey where they say, "Oh, no, no, we never use".

And people did experience some motivations to try to reduce where they could. You know, I didn't -- and people varied in how they -- some people didn't really

care at all, you know, and other people wanted to know how they could do it.

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MS. RUDEL: So moving on to matching messages to the evidence.

And I'm going to focus on the issue of risk-based guidance values for this, because I know that this is an important question right now in this room.

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MS. RUDEL: So this is an example of a report-back page. Can you see it? I don't know how well -- how visible it is there.

So this shows results in house dust for one participant for phthalates, PBDEs -- well, BFRs, brominated flame retardants, but real it's PBDEs mostly, and 3 PCB congeners.

And so I'm just going to talk through some of the observations, some of the things that I think about when I'm looking at this. Can you see the mouse?

No. I can't see the mouse.

Well, so the health-based guideline -- the health-based guideline values for dibutyl phthalate and butyl benzyl phthalate, we can see where they are on the graph. But what I know about them is that they, at the time that this was produced, they came based on EPA

reference doses. And so they were actually based on 1950s studies with endpoints of mortality or liver toxicity in one case, I think.

And so those are outdated. They don't really reflect any of our current understanding about dibutyl phthalate or butyl benzyl phthalate, how they work, the fact that they're antiandrogens, reproductive effects. We don't know -- I don't know where the new RfD would be exactly, but -- you know, if you did one.

And it also -- because now we know that many of those phthalates are acting additively, so it's hard to put a health based guideline value that adequately can consider then the person's combined exposure. You know, that would be a challenge.

With diethylhexyl phthalate, many people in the study might be very concerned, "Oh, look, every house dust sample is above the screening value for DEHP in residential soil. Why is that?"

Well, DEHP -- this is based on a cancer endpoint for DEHP for liver tumors. And where there's a lot of conflict in the scientific community about whether those are actually relevant to humans or not. And I don't know the answer. I'm not -- so I'm not saying that they are or they aren't.

But all of that information is not captured in

this little red X. It kind of -- I remember this cartoon, which actually I looked for on line last night. I couldn't find it. But there was like a tanker on the highway and it has one of those hazard signs on the back and it says, "The scientific community is divided. Some think that this is hazardous and some think it isn't".

(Laughter.)

MS. RUDEL: So what's the equivalent -- you know, what's the equivalent here that we can use?

So at the time we did this -- again, so we didn't -- there were no RFDs or cancer slope factors to develop health-based guidance values for the PBDEs. And so that can result -- you know, when there's missing information, that can result in lack of attention to something that might be worth paying attention to. So you don't see any health-based guideline values.

So if that's your frame for thinking about it, you're not going to highlight that. And, in fact, this person has actually some of the highest BFR exposures. And so a reasonable follow-up for them could be like, well, they might have an unusual exposure, so -- and that's something that's more actionable in a way or something to -- that's important for them.

There are some similar types of issues for PCBs with, you know, additive effects with other thyroid

endpoints, all the congeners not having the same toxicity, how you consider them together. All of those issues in thinking about how to do risk assessment for these compounds. And it's just -- I don't know how to capture that in the little red X.

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MS. RUDEL: So the risk-based guidelines, they're useful. We want some kind of a health-based benchmark. But the values -- the reference values are inconsistent, outdated, and incomplete. There are many, many assumptions required to derive kind of equivalent biological level values or bioequivalence from rodent studies, based on intake. And that leads to a lot of uncertainty.

There's insufficient data on population variability and pharmacokinetics and pharmacodynamics to capture that. And if you did actually try to capture it, then you are going to maybe end up with a range of concern levels that's so wide, it doesn't actually have meaning itself, you know.

They don't consider combined effects and they really fail to communicate the high level of uncertainty that's involved in their derivation.

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MS. RUDEL: This is a quote that I've always

liked from this the decision theorist. So these bright line approaches, while useful, they really can hide uncertainty and provide false reassurance. We'll find a variety of devices that allow ignorance to masquerade as knowledge, so that we can make decisions, you know.

(Laughter.)

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MS. RUDEL: So we've -- in thinking about matching messages to evidence, there are -- I'll back up actually for a second. So this is just -- I'm going to array some exposures based on how much we know about health effects, not how bad they are, but how much we know about them from little knowledge to more knowledge, and how much we know about how you could reduce exposures on the Y axis.

So lead and mercury, we have pretty good understanding of exposure or sources and health effects at least compared to some of the other compounds we're talking about here. And there -- you can match -- your message can involve a clear public health or individual action message.

Things like diesel particulate or current use pesticides, the exposure reduction is known because you can read labels and decide what you're going to use or for diesel we understand about health effects and trying to

reduce particulate from diesel is kind of a well accepted environmental health goal.

But some of these others kind of like -- we had banned chemicals like chlordane, where we do know a fair amount about the health effects, but I had nothing to tell the people about how they could reduce levels in their home. All I could find, in fact, was that the Department of Defense actually demolished defense housing that had high levels of chlordane, because they couldn't -- and then rebuilt it. You know, so I really didn't want to have to recommend that to anybody.

(Laughter.)

MS. RUDEL: So then things that are, you know, flame retardants, where the health effects were kind of in -- you know, we're working up to having more information, but it's hard for people to know what to do to reduce exposure. And similar issues with some consumer product kind of chemicals, like phthalates and so on. And so for these, we're saying to recommend -- you can recommend precautionary action if the person wants to take it and more research really, and to avoid ungrounded reassurance.

So I've been tempted many times to reassure people in these studies and really try to be fair, because it's just as misleading to suggest that something isn't a

risk when you don't really have data to support that, as to overstate the risks. So it's not a one-sided situation, it's a two-sided situation.

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MS. RUDEL: Now, on the exciting new idea, who's high and why?

I think that this is really going to be a key way to identify important exposure sources that we don't really know about and figure out which ones are important, to start to understand better about health effects, and to target interventions where needed.

And I'm going to demonstrate this by just telling you a case study or story from one incident in our study. So we had one person whose report-back summary looked like this.

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MS. RUDEL: "Your house was selected for retesting, because we detected high levels of PCBs in your air and dust. The levels of PCBs in your blood were...among the highest of 4,000 people tested in a national survey by the U.S. Centers for Disease Control. This suggests that PCBs in your house are an important source of your overall PCB exposure. We can't tell from these tests what the sources are in your house. PCBs were used in electrical equipment, like transformers,

fluorescent lights, and other products listed on the back of this page. At high exposures, PCBs affect thyroid hormones and brain development. Scientists have found that eating fatty fish is usually a significant source of exposure. Let's follow up with a phone conversation about this."

So most people didn't get the, "Let's follow up with a phone conversation", note at the bottom. And so we went back. This was 5 years actually after the first study, where we retested. The air and dust were high, quite a bit higher than EPA guidelines for residential soil or for ambient air. Their blood levels, everybody in -- there were 2 homes actually that we retested because they had high. And everybody in those homes was above the 95th percentile and NHANES age matched -- age and gender matched, except for one person who had just moved into the house about 6 months ago.

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MS. RUDEL: And so what's the source?

So, you know, we were in there and asking lots of questions and trying to look for all the things that -- I was talking to the EPA Region 1 Administrator who's telling me, you know, PCBs aren't a residential contaminant. So I'm like, well, we detected them in 30 percent of the houses, so maybe they are.

And the one family had lived in the house for a very long time. And the male head of household had done a lot of the work on the house himself. And so as we were asking about all different, you know, building materials and former uses and so on -- and this is Cape Cod. This is not an industrial area by the way. So he -- I asked about the floors. So they're wood floors and some of them clearly hadn't been finished, refinished in a long time.

So he said -- he actually remembered. He said, well, I remember the product, because in the fifties this new product came out and it was called Fabulon. And it was a floor finish that you didn't have to do the paste wax and waxing and stripping. It was a great product. It looked great, and it was expensive, which is why I remember buying it and using it. And I used it up until the late sixties and it stopped working. It didn't work as well.

So, okay. So we go back to the office and we look it up in -- and believe it or not in the 1957 Edition of Clinical Toxicology of Commercial Products, PCBs are listed right there as an ingredient of Fabulon wood floor finish. And so that was my ah-ha moment.

And then we started to wonder about opportunities for how widespread this was.

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MS. RUDEL: And we found advertisements from the fifties and sixties that the -- you know, this was a woman's liberation product obviously, because it did no more waxing, no more scrubbing. But it says down here in small print more than a million homeowners today enjoy the lasting beauty and protection of, you know, this Fabulon.

So this was an example of how following up is identified really, you know, a novel indoor source of PCBs. Many people, by this time, have sanded those PCBs off and, you know, refinished. And the levels are lower. And newer houses probably don't have this, but some schools and other buildings, and -- you know, and homes still do. It's low on time, right?

MS. HOOVER: Finish in a couple minutes and we'll have time for questions.

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MS. RUDEL: Yeah, I'm almost done.

So following up on high exposed individuals is -- well, it's responsive to individual expectations. That is I think that participants in the study might feel sometimes that if they have a particularly high exposure, that you, as the researcher, would follow up with them about that.

So it's consistent with the idea of a surveillance program. So you are doing surveillance to

understand from, you know, a public health point of view or from a research point of view. And looking at what's happening with high exposed people is consistent with those goals.

It can generate important new information. So who are the high exposed populations? It can help discover, you know, undocumented sources. It can really help this really important problem, which is describing population exposure variability, which, as Dana pointed out, is really quite substantial.

If you look at exposure distributions from almost any data set, they're very, very highly skewed to the right. And there's always about a 1 or 2 percent of the population that's way out in front of everybody else.

And those are the people, they're hard to find. If you're doing a health study, if you're trying to develop biomarkers of exposure, those people are hard to find. But these biomonitoring studies actually provide the way to screen out and then focus on the high exposed people.

And they highlight where public health intervention and study could be most fruitful, because that's where the action is. And we're actually in conversation with the NHANES folks right now about trying to do this. They've been a little bit reluctant to do --

you know, going back to participants, but they have indicated some willingness to talk about it. And anybody who's interested in this or think it's a good idea, like -- because see me, because it will help for them to have an indication of how widespread the interest might be in this kind of activity.

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MS. RUDEL: And so that's basically what I wanted to say and just emphasizing my main points, that if we review -- we should review the ethical frameworks in thinking about benefits, autonomy, and justice as well as potential harms. That we identified what people want to know and have made some efforts to try to answer those questions. That it's easy in communicating to do false reassurance. And so that's something to keep an eye on and figure out how to communicate messages. And especially the challenge, you know, is severe with risk-based or health-based guidance values around that specific point, conveying the uncertainty. And that following up with high-exposed individuals will be, I think, very fruitful.

So thanks.

(Applause.)

MS. HOOVER: We have 3 minutes for questions. So if anybody has any?

DR. PARK: I have a mic.
MS. HOOVER: Say your name.
DR. PARK: June Soo Park from the California EPA. Thanks for the very nice presentation. Also great study design, and fabulous collaboration group.
And 3 minutes, I have 2 questions. First of all, you talk a lot --
MS. HOOVER: Just one.
DR. PARK: Select one?
MS. HOOVER: Just ask one.
DR. PARK: The first question is you talk a lot about the sources, exposure sources. You found the one all on the floor touching. Have you worked with some, you know, the PCB emissions from the, you know, all the paint and the concrete work? They recently published, you know, that they might be another source in the indoor house.
MS. RUDEL: I'm sorry. I had trouble. I don't have great hearing.
DR. PARK: The PCB source.
MS. HOOVER: Are you asking if there's other sources in the house?
DR. PARK: Yeah, other sources of PCBs, yes.
MS. HOOVER: Besides the flooring.
MS. RUDEL: So there certainly may be other sources in the house besides the floors. And, you know,

we found this one. And we didn't -- we didn't actually test the floors. But one more clue actually that we had is that the home with the individual who was higher than anybody in NHANES, they had actually in the month preceding our resampling and blood sampling, they had sanded and refinished 2 floors in their house. So that was another kind of piece that I used in thinking about that.

DR. LUDERER: Ulrike Luderer, UC Irvine. Thank you very much. I really enjoyed that presentation. It was great. I kind of have a question related to the report back and the format that you used. So, you know, one of the things that I noticed was that you have this logarithmic scale. And I was wondering whether, you know, you had any comments on how difficult or not that was for people to understand, you know, when making comparisons both to other people within the same population and to the reference values?

MS. RUDEL: Yeah, I -- we did think about it a lot. It's really, because the data spans such a range, the only way to do it. And since really it just -- you're looking at your place in relation to others. We felt that it did basically kind of convey that aspect of the distribution.

DR. BARR: Hi. Dana Barr, Emory University.

Thank you for a great presentation, Ruthann.

I had a quick question when you talked about the 1 person who had blood levels higher than -- either it was at the 95th percentile of NHANES or anyone in NHANES, and was that derived from your report of from the raw data or...?

MS. RUDEL: Based on the raw data, we -- from the years that were most similar to the years when we collected the blood sample, and then we took the age and gender matching the people. So there were four residents living in 2 houses that had these very high PCB levels. And so all 3 of them were in the top 95th percentile. One was as high as the highest, and -- actually of anybody, but -- because it's an older woman. So they're higher. They're the high group, anyway.

And then only one of them was not in the top 95th percentile, and that person had just moved into the house a few months ago.

DR. BARR: I thought that you had done that. I wanted to actually just reemphasize that when you're doing those comparisons, especially with the POPs and NHANES, it's really important to go back to the raw data, because the way they're displayed in the report with the variable LODs, they don't report a percentile estimate that's lower than the highest LOD. So you could actually have a 50

percent detection rate in NHANES and have no median value there if it's above the -- if the median value is below the highest LOD among the groups. So I think that's a great thing that you did.

Thank you.

MS. RUDEL: Thanks.

MS. PATTON: Hi. Sharyle Patton from the Commonweal Biomonitoring Resources Center.

What a great talk. Thanks a lot. What were the legal ramifications of telling a person that they had high PCB levels in their home, in terms of their reselling the house and kind of information that they might need to know or not know and how did you deal with that? One question.

And just a comment. As you know, Commonweal Biomonitoring Resource Center, that's what Silent Spring sometimes calls judo biomonitoring, which I like a lot. And it's just to say that there has been a difference we found in communicating data into communities where people are giving blood or a biospecimen, just because they're doing their civic duty and they want to help science to a community who's absolutely convinced that a wide range of problems are caused by exposure to a particular chemical. So we've really had to work with that, and I'd love to talk to you about that later.

MS. RUDEL: The legal problems are problems. And

we've actually, doing some kind of extensive work with the Harvard Law School about how informed consents need to be crafted in order to convey the risks and benefits of getting the -- of getting the information, acquiring the information, because some assessments are that, you know, that it would rise to the level of something that should be disclosed on a sale. So that's an issue. It's not so much of an issue for biomonitoring of humans, you know, but when you're doing home samples.

DR. KYLE: Hi. I'm Amy Kyle from UC Berkeley. Thanks for your talk. I was wondering when you're thinking about the what you can do part, you know, on your graph and in your interactions with your participants, whether you think about it in terms of what like what I could do, in terms of my house, versus what could be done? Like what we could do collectively? I'm wondering if you make that distinction at all or how you think about that question?

MS. RUDEL: We do actually. We do try to provide both individual and social or policy level actions.

MS. HOOVER: Thanks Ruthann and all the audience. So I'll identify myself. I'm Sara Hoover from OEHHA. I just wanted to let you guys know that we're going to start back promptly at 10:45 on that clock, so we have a 15-minute break, and we'll look forward to seeing you

back.

(Thereupon a recess was taken.)

(Thereupon an overhead presentation was Presented as follows.)

MS. HOOVER: Okay. If everybody could take your seats, we're going to get started. Sorry, I've been repeatedly reminded to back off from the microphone.

Okay. So my name is Sara Hoover from OEHHA, and I'd like to introduce Dr. Tina Bahadori who's going to speak to us right now. And then after that, we'll be having our morning panel.

DR. BAHADORI: Good morning, everyone. I'm sorry I forgot to wear green apparently, but I look ethnic so that should count.

(Laughter.)

DR. BAHADORI: First of all, thank you very much for inviting me to this meeting. As I was telling Sara and Lauren yesterday, I feel like I'm in a foreign country. Living in Washington, in case you didn't recognize our little monument there, just the world is very different and the issues are addressed very differently. And I'm sort of very glad to be here. It's been a real grounding experience.

So I'm going to start with a little bit of obligatory materials up front, tell you where I'm from and

what I'm doing.

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DR. BAHADORI: And then I'll get into some of the more, sort of, emotional perspectives.

One of the questions people ask is why are you here and why should really industry care about this? And I think what has really become apparent and we've worked very hard to really communicate this to our executives and the people who provide funding for our research programs, that industry is really apart of this issue and we play a vital role and we have a vital responsibility to join in the dialogue that's a topic of this workshop and has been a topic of several workshops that actually I've personally organized and some of you in the room have helped me put together.

As a body, the American Chemistry Council represents companies that employ actually nearly a million people even in this economy. And it represents $670 billion of enterprise investments. So with that comes an obligation and the responsibility. And this is just -- these are just U.S. numbers.

And that really, because we are a science-based industry, because chemistry is the fundamental of what we're doing and what biomonitoring is really all about, that there are really opportunities, and learning

opportunities, here that really need to be taken advantage of.

And from our perspective, really the future of our product innovation, the future of our contribution to the society is tied very closely to the outcomes of the activities, like the California Biomonitoring Program, like the NHANES program, and like a lot of the much needed exposure measurement programs out there.

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DR. BAHADORI: What is the LRI? I'm the managing director of this program, which the Long-Range Research Initiative. It would like to be long-range. When you're in Washington, long-range is anywhere from 5 minutes to a year. But I try to stay ahead of that game where possible.

(Laughter.)

DR. BAHADORI: It's a program that's funded by the American Chemistry Council. The money comes directly from the industry contributions to the organization. And it's designed to find that intersection of issues, like biomonitoring, that have high value to the society, but also have high relevance to the chemical industry. And the idea is to sort of advance the science to get a better understanding of how biological mechanisms are affected by exposures to chemicals.

Obligatory. This is how we run the program. It's basically a very public and open program. It's almost -- the majority of the work is either done in the universities or through collaboration with our NGO partners. The work is published. Everything is in the public website. And I'll show you that later.

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DR. BAHADORI: It also a global program, so the investment is actually pretty significant when you think about the work that's done in Japan and Europe and in the U.S. the focus is a little bit different. In Japan, there's a lot of emphasis, even the biomonitoring work is focused on multiple chemical sensitivity, issues related to indoor exposures.

In Europe, this whole energy efficiency issue has really affected a lot of their focus on the types of studies that they do. And they do a lot of models, because of the regulatory driver of REACH. They do a lot of models-based research and then a lot on chemical sensitivities.

And in the U.S., we have sort of a mixed program, and I'll explain that in a minute.

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DR. BAHADORI: So in this year, but this is probably a fairly typical, sort of, distribution of our

research, the bulk of the science in our chemical industry companies is really focused on toxicology. They call it health sciences, but it's really toxicology.

So since that's where the energy and the momentum comes from, about 60 percent of our research is really focused on toxicology, but it's really looking at moving ahead away from traditional and more toxicologic to the extent possible and looking for innovative and more efficient ways that give you more information in a more timely fashion about chemicals.

So it does involve looking at a lot of the genomics, toxicogenomics. It does involve a lot of investment in the high throughput assays and interpretation of data from that.

But what's new is that we were able to persuade our CEOs and the people who give us the money that all of that hazard information is only like a one-handed animal. That without the exposure information, it's going to be impossible to contextualize the hazard information, and more input needed to create interventions, and to understand what is it that's causing those effects and what needs to be done.

And about 10 percent of our research is involved in outreach and translation. And what that means is that we were doing really well going along, doing a lot of

research and publishing it out there in literature. But you put it out there, and you just pray to God somebody makes eye contact with the paper and does something with it.

So what we found is it is really difficult to use science for decision making, unless you hold meetings like this, where you bring people from different backgrounds and different technical expertise, and have these conversations and the lessons learned from people who've been doing this work for a long time, about what's working and what's not working. And I'm going to explain in a minute, how does some of this effort really help shape our program, from where you are today to probably a very different direction than where we are today.

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DR. BAHADORI: I also want to say, I mean, my bias is as, that you may have heard Dana is the current President of Society of Exposure Science, and I'm her immediate past president. There is a bias here.

To us, biomonitoring is really a surrogate for exposure science. And why is it exposure science is important? It's because it creates that bridge between the exposure to chemical, physical, and biological agents, and ultimately health. I mean, we don't care about exposures for the sake of exposures. There's a context of

health here.

And I'm not just talking about risk assessment, I'm talking actual health and the impact on health. And that there is a foundational -- exposure sciences is a foundational element to understanding that interaction between environment genetics and health.

In this country, we've made a significant investment in the human genome project, in characterizing genetics genomics, but we've completely left behind the science, the commensurate science that describes how the environment can influence these relationships and what role the environment plays.

And many, many recent studies have demonstrated that the genetics alone explain a much smaller percentage of the health outcomes that we're seeing, that there's the more important impact is environment, but really the interaction between environment and genetics.

And again -- so our sense is that biomonitoring alone doesn't really capture that information.

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DR. BAHADORI: You've seen this before, I just wanted to sort of say that this is really a continuum, and that exposure is a component in here and biomonitoring is a component of that.

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DR. BAHADORI: So why does it matter? Because it is really a crucial component to understanding health. It puts the hazard data in perspective. If you don't know what exposures are occurring, when, where, and how -- and I'm not just talking about occupational exposures in a facility, I'm talking about incidental, and really if you think about it, is the collateral exposures, is what we call it. Exposures that occur when people aren't even aware that what they're doing is creating an exposure.

That's the challenge, and those are the ones that are contributing to this conundrum of understanding chronic health effects that we didn't really understand in the past.

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DR. BAHADORI: The other issue is that within the field, within the work that Dana and I have been doing, we really are pushing to move away from this reactive science, from reactive public health policies that basically are ready to pounce when big old disasters happen. And even when they happen, like the oil spill that we had about a year ago, we still really don't know what to do.

What we're trying to do is move the science to be nimble predictive to be really protective in the true sense of public health protection, and to help with

disease prevention. So that's sort of the motivation for a lot of the work that we're doing.

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DR. BAHADORI: This is a slide that actually Sam Wilson, who was at NIEHS at the time really presented to us at one of the meetings, maybe about now 6 or 7 years ago, where he was trying to sell why biomonitoring was really a good investment to make -- that absent, you know, other information, that it provided really good linkage to move from data that often -- for example, EPA collects data at regional and national city level. Some enterprising scientist with a little tiny little grant does a little bit of community level. Some enterprising NGO goes in there and actually gets into the environments where people live and spend their time and their children crawl around on the ground and do some additional measurement, and then we pray to God that somehow with that little device that hangs on you, for 4, 8, 12 hours, that somehow you have, by some will of God, have now captured exposure information. And his premise was that that's just simply not efficient.

So he was arguing that biomonitoring is -- at least it gets you a little bit closer and it gives you more information about exposure.

But we argued with him that biomonitoring tells

you what's in the body. It doesn't tell you when it came from, where it came from, when it got there, how often were you exposed, how long was the material residing in your body?

And we insisted to him that what we really need is more exposure information. He said, I agree, but really look. Exposure science has been really remiss in providing efficient and effective tools that can provide the commensurate information that you need to answer it with the biomonitoring data. Even if we agreed we need the data, we don't have the tools to efficiently collect it. On a population level, we can't do it.

I mean, my dissertation was built on measuring 10 people that was really brilliant, but, you know, what do we do from that?

And it's been really difficult to connect the dots that we know need to be connected.

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DR. BAHADORI: So biomonitoring for us also, as well as this program, has served as a surrogate to answer some of the unanswered questions, even with understanding what all the shortcomings are and what are all the ways that we could do things better.

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DR. BAHADORI: So we -- you know, as program, we

supported even developing novel biomarkers, more efficient analysis of biomarker data. We invested in studies that look at issues related to limit of detection issues, regarding do you pool samples, do you not pool samples?

So in our first iteration, I'm talking around 2006-2007, we need a lot of investment in sort of advancing that science. But then quickly we're where you are today. We couldn't articulate the relevance, especially as industry. If we had the biomonitoring data, there was an expectation that we knew what the heck it meant. Well, clearly, we don't in most cases.

And it was very difficult to understand the questions related to exposure frequency, concentrations and pathways. And then really to understand, if we took a sample and something wasn't there, does it mean that the exposure actually didn't occur or did we just miss that window when we took our measurements? So that ended up being a big issue that continued to plague us.

But because it was such an opportunity, because it helped us populate that black box, when people asked you what do you know about exposures, we can say, oh, look at the NHANES data or look at this. At least it gave us something to say. And it was really a better, faster, cheaper method to collect, you know, in a more prevalent way the data that was needed.

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DR. BAHADORI: But of course, as we all know, and as we heard from Dana today, exposure is dynamic. I'm going to be using some of the slides that Steve Rappaport and I developed for a workshop that we did for the National Academies earlier this year -- no, early 2010, and we're going to be repeating some new information later this year.

It's very clear that levels of both exogenous and endogenous chemicals vary within and between individuals and across populations. This variability can be, at times, 10-fold or even Steve Rappaport has data that shows it can be up to 10,000 fold. That type of variability is very, very difficult to characterize or to predict without having actual empirical data, and without collecting that data in a longitudinal study and through repeated measurements.

So these wild samples serve a purpose. They have tremendous value, but they're not really sufficient to do health risk assessments and they're not really sufficient to do -- to characterize information that you really need to create effective interventions.

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DR. BAHADORI: So the concern became again, looking at NHANES, is that we're generating volumes of

data, but we're not really making -- not as a nation and not as an industry, we're not making the comparable investments to interpret the data. And without this investment in interpretation, there was almost a sort of an ethical obligation to understand then why are we collecting these samples if we can't really do what we need to do to be protective?

So we held a workshop much like this in 2006. And it was in Minneapolis. It was a transdisciplinary workshop. We brought a lot of people together from a lot of different fields. And we quickly learned that the questions were far more complex than we were equipped to answer.

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DR. BAHADORI: The next year, we held another workshop, this time with EPA, to say okay, maybe we can't do, you know, risk assessment. Maybe we can't do exposure intervention. But maybe, if we're creative, we can do some public health interventions. Maybe it can tell us something about trends. Maybe it can tell -- yeah, so it tells us something, but it doesn't really tell us enough to do what we need to do if we really want to understand the exposures and want to mitigate them.

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DR. BAHADORI: So from those 2 workshops, it

became clear that we needed to increase the resources devoted to exposure studies that included biomonitoring to actually -- that had to be done consciously. It couldn't be an afterthought.

You really had to think about what are you trying to do with your biomonitoring data, and make the commensurate investment to characterize the totality of the paradigm to contextualize the real world exposures, and to understand the human element, the intra- and inter-individual variability.

And to make that investment, to understand how that can be tied into risk assessment and to move away from the sort of studies that inform you about a small population and see how you can extrapolate to population-based data.

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DR. BAHADORI: So we then quickly put out a group of RFPs that we started looking at how do we go about characterizing predominant sources and pathways of exposures for susceptible populations. And again, I'm talking about what we would characterize as incidental exposures.

To look at the relationship between environmental contaminants and biomonitoring, and then to develop sort of more holistic methods, better PBPK models, better data

for those PBPK models, that tell us -- give us more information about dosimetry and give us more information about dose at that relevant cascading level of the biological entity at the human level.

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DR. BAHADORI: But we quickly found that that was difficult to do, because even a million and a half, $2 million for an exposure study didn't really go very far, and it came down to just characterizing a very small population. So we said okay, let's look at the literature out there. We saw that there's a comparative toxicology database, that was developed as a product of an NIEHS grant, cost about a million dollars a year...where scientists up in Maine, they hand curated data from published literature, where there's information on gene, the presence of a chemical and a disease. So if those 3 components exist in a paper that paper gets hand curated into the database.

So we met with the investigator and we asked, well, why don't you have exposure information? Why do you just have environmental concentrations? He said -- she said, exposure, what's that, and where is it? I've never run across it.

So we produced a bunch of papers, and we told her to look at it. Some of them I think were actually

Ruthann's papers. And she said, "Huh, I've never seen these papers".

So it quickly became clear that going back to what Dana said initially, there is an incredible language and conceptual disconnect between the people who do exposure studies and the people who do health studies. And biomonitoring people tend to come mainly from the health and dose side of the equation and less from the exposure side of the equation.

So this disconnect meant that they weren't even looking at each other's literature, and that -- given the paucity, I mean, that almost seemed criminal. They won't even look at what's available or that people have data. They've collected data, but there were never sufficient resources to analyze the data to make it publicly available to incorporate it into a part of a larger picture, because often the people who are running around doing measurements, don't get around to doing anything beyond the rudimentary analysis that helps you describe the data. They don't get to do the more sort of complex and more interesting analysis that allow you to look across maybe a meta-look at a bunch of other data and get information in other ways.

So we created this ontology project, which was a relatively small effort, to take this NIEHS grant and

create a language that helps you connect the exposure data to this. And that project was just completed and the paper was submitted. It doesn't mean that there's any exposure data in it yet, but we just created the translating machine at this point.

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DR. BAHADORI: The other thing that we did, we're led by a biomonitoring sort of investment. And Lesa is going to talk later about the Bio -- the BE project, which actually wasn't funded by my program, but was very informative. And Lesa took that work and collaborated with ToxCast Program to try to make sense of some of their dosimetry data, and she'll talk about that later.

But one of the things that we did in a related manner is we took the work that was going on at the National Center for Computational Toxicology where these assays were being used for Phase I chemicals, which was mainly the really well characterized mostly pesticides or related inerts.

So we took the assay data from that and we worked basically from the NHANES data to see if we could reconstruct the oral dose equivalent from the biomonitoring data to get a sense of where the exposures fell within the -- so each one of these box plots for each chemical shows the range of effect that was observed from

those high throughput assays that were being used by ToxCast.

There's a lot of questions about whether those assays are, in fact, relevant. But that was what EPA was using to determine whether there are effects associated with a particular chemical. So we took those -- this represents the effects seen at the various levels, because they're able to test at various levels.

So we took the NHANES data and reconstructed the oral dose equivalent, and demonstrated that for the majority of the Phase I chemicals that the population level exposures, as represented by NHANES, was, in fact, for the majority of those Phase 1 chemicals, again well-characterized chemicals, was well below, for the majority of them, for any level at which any effect was being observed.

There's some exceptions, like triclosan that then resulted in additional testing and studies. Now, there's a lot of issues here. We know what the issues are with the NHANES study. We know what the issues are with these assays. But this was a first attempt at doing, you know, connecting these big databases together.

So since that worked so well and we had a good understanding of that set of chemicals, we moved in and we just started a new project to look at the Phase II

chemicals, which is primarily consumer chemicals about which we have very little NHANES or otherwise exposure information. So the true test of our creativity will be what we can do here. And this is a project that literally began just a month ago.

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DR. BAHADORI: But the project that I talked about the work that's done has already been published. As you can see, it's a collaborative effort between EPA and a number of people that you may know well.

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DR. BAHADORI: So I'm just going to wrap up -- I was just given the 5-minute sign -- to show where we're going with our research. It has become really clear that this sort of measuring exposures, whether through biomonitoring or through environmental exposures, sort of measuring exposure for the sake of exposure wasn't really going to get us there.

So there was a workshop earlier in 2010 that introduced this concept of the exposome, where Christopher Wild, who is now the head of IARC, the International Cancer Research Agency or something like that, recognizing the disparity and the current knowledge between genes and environmental exposures. Chris Wild defined the exposome as representing all environmental exposures, including

those from diet, lifestyle, and endogenous sources from conception onwards as a quantity of critical interest to disease etiology

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DR. BAHADORI: He put that out as a challenge saying if you really want to do this right, we really need to create a paradigm shift, where the exposome is everything from all these sources, though we don't really go there and just measure things and not understand in the end the collective impact on the body, the cumulative impact on the body. And the exposome gives you the ability do that.

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DR. BAHADORI: It also, if done right, and even within this exposome community, there are people who are primarily focused on the measuring what's inside the body. And then from that, trying to extrapolate what could have happened outside the body.

And then there's people who are focused on what's going on -- you know, doing these detailed characterizations of what's going on outside and then try to see if they can link it to the biomonitoring or the otherwise biomarker data.

The proposal of the exposome is for the community to really work together and to bring these concepts

together in a more thoughtful way, so that we're not always working under the lamppost that we like with a particular hue of light that we like, but we do this more collectively.

So taking the lead from this effort, we actually started the project late last year, which begins to look at some of these novel biomarkers of the exposome, in these cases, to characterize endogenous and exogenous levels of PAHs. And then to make sense of it, we created a collaboration between the study at Berkeley and the work that EPA was doing character -- of doing biomonitoring of blood and urine from the MICA study, which is children's asthma study, and trying to see if we could reconcile our observations between these novel biomarker data that are collected really from a simple blood spot to the more larger scale observational study.

So we have great expectations from that project, and I believe the first paper from that will come out later this year. Although, since that's a continuation of a lot of the work that Steve Rappaport and Martin Smith have been doing at Berkeley, there certainly are a lot of related and relevant papers that have come out in the past 4 or 5 months.

So I'll just conclude with a little bit of shameless advertising. We have a workshop coming up in

June, that we're doing in collaboration with Health Canada that is really addressing this issue of advancing exposure science to improve chemical safety, whether it's biomonitoring, exposomics, we hope to address it in this way. And, of course, Health Canada has a lot of experience looking at this topic of characterizing exposures, and also the biomonitoring issues that they've been working on especially with children.

--o0o--

DR. BAHADORI: And then I alluded earlier to our website where a lot of our information is publicly posted. And that's where the website is americanchemistry.com/lri.

--o0o--

DR. BAHADORI: And the finally I just sort of want to go back to the point I made earlier that we have found that really it's in these workshops and in these sort of gatherings like this that you really translate the science and you really make some useful collaborations come out of these meetings, and that create opportunities that don't exist when you just sort of throw that publication in the wind and hope that it lands somewhere interesting.

So that's it.

(Applause.)

MS. HOOVER: Okay. We have a few minutes for

questions for Tina, so if anyone has questions. Also, I forgot to tell people on the webinar that you can Email questions to biomonitoring@oehha.ca.gov. And we can read your questions aloud.

So any questions for Tina?

DR. ZEISE: Very nice talk, Tina. Thank you.

Could you say a little more about where you see the research going on translating data like in ToxCast into comparisons with biomonitoring exposures and what your plans are in that regard?

DR. BAHADORI: Yeah. So a significant part of our research over the next, I'd say maybe, 5 to 6 million -- that's significant to me. It may not be significant for others but -- is going to go into that translation activity. So we have got several pockets of research are in there. One is this Phase II analysis that we said -- that we're fairly sure NHANES is not going to give us everything we need for the consumer exposures, but we're going to use NHANES where possible. We have access to some other biomonitoring data, and we're going to use that. And then we're going to use our -- we have another project going on where we're trying to reconstruct exposure indices.

So we may not be able to model exactly exposures, but we can get ranges or indices of exposure that tell us

enough, so that we can tie it back to the ToxCast data and marry the exposure indices with the toxicity indices and try to see if we can make those connections.

Now, as we get data richer, as we do more measurements, as we do better models, we can come back and enrich these indices and make them closer to reality. So we have a ground-truthing exercise that actually Bette Meek who was at Health Canada, now who's at the University of Ottawa is going to lead in helping us ground truth as more data comes in through our other studies or through our exposure modeling efforts, how much does it really only make those indices a little better. It's the same question as is biomonitoring close enough to what you need to know about exposures? And she's going to help us with that ground-truthing exercise.

We're also starting to work -- this is also work that we're doing with both EPA and NIH to try to see how much of the data that we have, either from the biomarker studies or from the hazard data that's coming from ToxCast can be used in actual risk assessment, and how close is close enough again. If you are able to move away from the more complicated and difficult to do animal studies, are there some set of chemicals that you know enough to be able to make some decisions about, because of course we can keep going forever.

But the premise is that there are some things that you can just lay to rest if you would get some consensus around it.

So as you see, it's really -- so the contribution, Elaine Cohen Hubal actually described our program as catalytic. So we don't have the resources that we used to have, $25 million dollars a year, to do a lot more, sort of fundamental research. But that was really difficult to demonstrate the value of.

So now we've gone into these areas where we're trying to take the data and actually make sense of it and use it towards decision making, which is the point of that last arrow.

And I actually have a table that summarizes our current research and I'm happy to send that to you actually.

DR. BRADMAN: Asa Bradman from Berkeley. I have one question and one comment. The comment I just want to underscore, your mention of the need to look at within and between variability. And an issue that I think we need to consider here in the program is how that affects report back.

You know, for example, some of the work we've done, we've seen order -- you know 2 order of magnitude changes over just a couple of days, which means that, you

know, reporting single measurement back to someone, the measurement itself is, on an individual level, is basically meaningless. On the population level though it probably has some meaning. So I think that is an important issue.

The other question I have is, does the ACC and your program have any thoughts or positions on reporting results -- individual results back to individual participants, in studies like this and providing interpretation and guidance?

I know one concern I have about this program or any biomonitoring program is that that becomes -- you know, when you get into the realm of risk assessment health interpretation, it can get extremely complicated, especially with many different kinds of compounds. You have reconstructing doses. You have high variability. And I'm wondering if your organization has thoughts on how that should be communicated.

DR. BAHADORI: Okay. So with regard to your first point, I completely agree with you. And, in fact, Lesa has a project that has a -- is just beginning, that's actually going to try to characterize some of that variability given the data that she's been able to lay her hands on, and address that question.

As you said, it's really relevant when you talk

about individual level exposures. It's less relevant -- she might actually be able to prove that it's actually equally relevant on the population level, but you might be able to fudge around when you're talking about population exposure. But certainly at the individual level, the variability is very important, and she's just starting a project looking at that.

But with regard -- I mean, certainly the position of the industry has been that communicating individual level exposures with this amount of unknown is -- you know, it creates responsibilities that are not -- can't really be met. They can't be met by us and they can't be met by the scientific community.

Of course, we get push back with the fundamental question that if you have that data, would it be more responsible not to communicate it at all?

And since I'm on the research side of the program, I get to grapple with these same issues very well. But certainly the position of the industry is that it really needs to be contextualized. It needs to be explained. Where we know something about the risk assessment, and Lesa is going to talk a little bit about that, we ought to be able to put it in context. And where we don't know, we have to contextualize and be honest about the fact that we don't know. But that's really no

comfort to the person who's receiving the data.

MS. HOOVER: Okay. I think we'll go onto the Panel part of the morning. So if Ruthann, and Dana and Tina actually, don't leave, come on back. We're going to have the 3 of you sit up here.

And we wanted to just start by letting the 3 morning speakers have a chance to say anything they want to say from having heard the other speakers. So just take a seat.

And, Dana, did you want to start off with any comments about the morning?

DR. BARR: Yeah, I think so. First of all I'd like to commend the other speakers this morning for excellent presentations. I think that they both hit on very interesting topics. One being, you know, what kind of information do we give back to participants and how do we reliably put that into context to avoid harm, to avoid unnecessary concern. And I think that that's a great thing that Ruthann has been working on.

Of course, you know that I've been working fairly closely with Tina on trying to come to graps --

DR. BAHADORI: Grips.

DR. BARR: Grips, thank you -- grips with this exposome concept. And we've got some ideas on how we can move that forward. And I think it's really a progressive

way and a holistic approach to try and get at human data and how those human data relate to changes in our body and disease. And not just external exposures, but especially including endogenous exposures, including stress, dietary exposures, exercise, and everything else that has -- that will have some sort of an impact or interrelation with our chemical exposures as well.

MS. HOOVER: Ruthann, did you want to comment on the morning?

MS. RUDEL: Well, I just -- this is a frontier. I think it's a little bit almost, not quite the wild west, but it's close and there are a lot of opportunities and a lot of challenges. So, you know, California is in the vanguard again, and gets -- you know, I think there's some really great things that can come out of this.

And I think especially thinking of the ways to use the biomonitoring information for something for a greater end than just knowing the levels. And so tying it to other questions that we need to answer in order to understand health effects.

And I'll go back to for example the idea of following up on high -- and also even just thinking about high exposed individuals and incorporating that into the presentations. In fact, when I was -- during -- Tina, during your -- one of the slides that you showed, which

was from the Rotroff paper, I guess, with the -- so it shows a box and whiskers for the outcomes of various in vitro ToxCast assays adjusted for some -- it's adjusted for some pharmacokinetic parameters.

DR. BAHADORI: Yeah.

MS. RUDEL: And then -- but then the exposure numbers is a dot and --

DR. BAHADORI: Right.

MS. RUDEL: -- it needs to be more than a dot. You know, I think the health effect information and the exposure information both need to be distributions. And on the exposure side, it's -- even, I know, you know, we have a tradition in risk assessment of thinking about like the median and the 95th percentile. But, in fact, when I see from distributions is often the 95th percentile is actually fairly close to the median. The skew is so great that it's the 1 percent.

And it can sound like, oh, it's so extreme to think about this top 1 percent, but that's actually a lot of people. And so I keep coming back to that the action is there. And then -- and I think we have a lot to learn. I think we can identify some, you know, early effect markers, and really, I think, from studying that group really start to get a handle on when -- you know, what level of exposure you do start to see effects in, and

whether things are relevant to humans or not relevant to humans and so on.

DR. BAHADORI: So actually 2 points. One is the thing that you pointed out is a major source of embarrassment for us. Because we went out, we made a big stink with the NCCT to say, oh, you're going to do -- basically, you're just replicating high throughput toxicity for these cells and what are you really achieving? You know, nothing about what a relevant exposure is. And so they came back with a robot that they now have that can measure anything you want in five minutes for 1,300 chemicals.

So they said, great, just tell us what exposure, what doses should we do? What are relevant population exposure levels? I said, it beats me. I really don't know. We didn't have the data. We had some models, but we didn't really have the data to tell them what relevant consumer incidental exposures were. Not that occupational levels are irrelevant, but we know more about those and we know less about the consumer exposure.

So they took a set of doses, I think they did 15 doses, to what looked low enough to them. But as you saw, that low enough was still much higher than what we're able to measure in NHANES. And those were really single data points. So that was really embarrassing and thank you for

pointing that out.

(Laughter.)

DR. BAHADORI: The second thing I wanted to say is that really you are in the vanguard of this effort. And just whatever we do on the east coast, we always invite people from California to come and tell us what to do. So you're right here. If you're going to start and really invest even in these meager times on this Biomonitoring Program, you ought to really get together -- this Committee should get together with people like Steve Rappaport and Martyn Smith, who have been doing a lot of work on this exposome, to see if there are leveraged opportunities. Not to replace what you need to do through the Biomonitoring Program, but to see if there are additional ways in which you can advance the frontier of the science.

Steve looks for the same blood spot level and he has less of a confounding from his papers. He's been thinking about this for a long time. So I think, you know, getting some discussions going through that expertise. The work that Asa has been doing, the work that Tom McKone has been doing from the exposure side, I mean, you have a wealth of knowledge here that could really inform the program in a more, sort of I think, dramatic way.

Again, you're already in the frontier of the health policy side, but I think you would also be in the rocket science end of the science, because you have the right people here.

MS. HOOVER: Okay. So now I want to open it up to questions from the audience. And if anyone on the webinar has any questions. And feel to ask questions of any speaker.

DR. MARTY: Hi. Melanie Marty from OEHHA.

As you guys were talking about the exposome and all this monitoring data, the question that I really have boils down to what kind of data are available for these exposome particular projects that evaluate early life exposures, like, you know, cord blood, breast milk, meconium? You know, to me there's not a lot of information about that out there. So what are the approaches to getting at that? And also to getting at exposures during puberty, because, I mean, you know, in my mind, the whole thing is windows of susceptibility, most important.

DR. BARR: I'll be glad to start on that. I think that there are a lot of -- or there are a growing number of data sets out there looking at exposures during the fetal period at using either the mom as a surrogate or cord blood or meconium, and early childhood exposures, and

even adolescent exposures.

But none of them really are using this holistic approach. Most of them are biomonitoring, measuring single chemicals. As Tina had mentioned, looking under the lamppost. And I want to take it a little step further and just say looking under lamp -- not even looking under the lamppost, but looking under the camera flash, because it's a snapshot of exposure in time.

And so I think that what we need to do is take some of these matrices, like cord blood and we can do some of these exposomic types analysis that Steve Rappaport has been doing and reporting, and trying to look at markers that -- or any kind of chemicals that are in those matrices that are perturbed in relation to exposures to, you know, various chemicals and other stressors.

And so I think, as Tina had mentioned, you've got a great opportunity here in California. You've got the tolls. You've got the scientists. You've got the funding. And you're in the forefront of most of the other states -- well, all of the other states, maybe along with New York, in trying to do this type of work. And so I think that you have the opportunity now.

So exposome data has just been generated in a few labs. The concept is really just catching on, but we'd like to see it kind of catch on and move exponentially,

because the ability to get at this kind of information could really move us forward fairly quickly, and exposure science and understanding the role of exposure and disease.

DR. BAHADORI: And to that point, Melanie, in fact, later -- I hope it will be December of this year. It may be earlier spring of next year we're going to do another workshop as a follow up to the exposome. The first one created an incredible number of conversations and a minimal number of collaborations, not because there wasn't the will, but there are no resources. Everybody got really excited, but nobody pulled out a checkbook, including NIEHS and EPA.

And really the idea was to really marry the biomonitoring studies, the exposure studies, and these omic studies. And they're all after the same thing. They're coming at it from different angles. And some incentive for collaboration really would make it possible. So we're going to do this next workshop in December, hopefully. We'll be looking at what are the data sets out there and what are the technologies out there.

There's a lot of new work. I don't know if you saw in Nature -- an article that was written by a nature -- it wasn't a science research article, but it was an article that looked at how some of these

technologies -- and it talked about the exposome, but it also talked about the kind of work that Mike Jerrett does with the GPS and all -- so it talked about how there were these opportunities to marry these. And this came out, I think, February 17th the issue of Nature, if you look under one of the perspective articles.

So it's just slow as molasses. We just have to keep doing this and keep making people talk to each other. And one of the issues was that we kept talking about national level investments. That really shut people down. We couldn't even get a conversation with Dr. Collins about this, because he's busy reorganizing NIH and doesn't really have the resources.

So we thought we'd bring it down a little bit, and talk about even how smaller investments that enable these collaborations, enable sample exchanges, enable bringing the Europeans here to see what they're doing, would help. So we've sort of taken our rhetoric down a little bit and hopefully it will be less scary.

MS. HOOVER: Okay. Ruthann, did you have anything to add?

Okay. Just offering you the chance to say anything.

MS. RUDEL: No.

MS. HOOVER: Okay. Any other questions from the

audience?

George.

OEHHA ACTING DIRECTOR ALEXEEFF: Hi. George Alexeeff here from OEHHA. I want to thank you all for your thoughtful presentations. And I've been sitting here, and I've been -- we have this cumulative impact project. And now I realize when I go to presentations and symposia, I get cumulative evaluation in my brain and all the presentations start combining and coming up with new ideas and things.

So I was thinking of Dana's presentation about -- and you had mentioned a comment about -- well, it seemed as you were saying that most of the exposures were from dietary exposures or personal exposures. I wasn't really sure exactly. So I was wondering if you could clarify that, because you use the example cotinine, and you used, I think, another -- you were talking about relative concentrations.

But one of the concerns that I have is environmental contamination through dietary exposure. Like we have a fish advisory program, and so there's a lot of, well, primarily methyl mercury, but there's other contamination as well. So dietary exposure to us is, in many ways, an environmental exposure.

And the only project -- the only kind of activity

that I'm really aware of that tries to go back and address this kind of issue of these cumulative exposures in a complete -- well, relatively complete way is this whole TMDL approach. At least we have -- we have advisories, fish advisories, that therefore then claim a waterbody is now impaired. And now there's required for regulatory bodies to figure out what are all the sources of that methyl mercury that's going to that waterbody that's impacting that fish, and then go back and try to, you know, address all those different sources. That's kind of a very cumulative thing. And it's very rough, as you can imagine.

But I was just wondering if you know of any projects that are trying to think of exposures that way, where they basically kind of cumulate into a dietary exposure, because we've been -- I've been very concerned from the beginning of when we begin with our estimates of dioxin exposure to infants through breast milk. And to me, it's a terrible confounder, where you have this great nutritional source and it's contaminated. And, you know, you don't really -- you'd like that there be no contamination, so, you know -- but you don't -- so you have to inform them, but then you might scare them from actually doing something that's really, really important.

And you can say the same thing with fish too.

It's a great nutritional source. And at the same time, you're now basically introducing a compound like methyl mercury, which basically is working opposite of what the nutritional source is doing, or anyway. So I don't know if you had any comments on how we could go back and look at exposure sources that feed into an exposure.

DR. BARR: I'm thinking also breast milk comes to mind when you have these matrices or these foods that are nutritious but yet have potential environmental contamination with it. When I was talking about diet, I was talking about diet in a broader sense. Not just the methyl mercury, not just the pesticides in water, but the dyes in your food, the -- everything that you get that can produce some kind of a species that can react someway in your body that have either an adverse outcome, a positive outcome or some synergistic outcome with an environmental toxicant or another component in the diet. So I was talking about it in broader terms.

I don't really know how to address -- I mean, we deal with this issue with breast milk a lot.

DR. BAHADORI: But there are projects. I mean your question was are there projects? Yes, I mean, certainly. I mean, Tom McKone is in the room. I saw him walk in --

DR. BARR: He's over there.

DR. BAHADORI: Tom.

(Laughter.)

DR. BAHADORI: Tom has a number of projects that are actually starting to do that. Again, a lot of them ended up being primarily computational that are now being populated with data as they become available.

So one of the challenges has been to locate the data and then make them usable for these models. So some of that work is going on.

There's also some smaller measurement studies going on, but they're not really as comprehensive as they need to be, because it's just too expensive to do.

Yeah, so there's, you know, a wee bit of work going on, but better than nothing.

MS. RUDEL: And I'll add to that, that I have another kind of new favorite study design, besides who's high and why, and that I think can be really informative about source apportionment of identifying, you know, do you have the big one or not? And those are intervention studies where -- following some kind of natural or intended experiment.

And there are a couple examples from the literature recently, and one that we'll be releasing in the next couple weeks, but Alex Lu looked at kids -- these are -- they don't cost a lot of money in many cases, and

you can do them especially for rapidly cleared compounds, but -- so he enrolled a set of kids who ate -- who normally ate conventional not organic produce. And then provided alternative -- provided organic produce and grains for a period of five days, and then they went back to their normal diet, and measured daily urines on them. And so for various pesticides, in fact, you can almost see the grain ones versus the vegetable ones and so on. You know, you can really get a good sense of the relative importance of that source.

There's another kind of similarly designed study that collected urine samples from people who were going -- I think it was a Japanese study -- going to a Buddhist Temple stay for a set of days. And then they could see change in the antibiotics that are used in fruit -- meats.

And so those are studies that actually can be done sometimes relatively cheaply. And if you pick the right -- you know, there's a gamble, up front, but you have to have some information to pick the right exposure and the right population and so on. But I think we should spend some time thinking about opportunities there, yeah.

DR. BARR: And just one comment to follow-up on Ruthann's. I mean, that work really did well to allow us to look at exposure. But if you're wanting to look at the impact on the body, then you may want to design a study

where you take longitudinal samples of people, blood samples for example, prior to consumption of fish, after consumption of fish over a period of time and look at perturbations in the chemicals that you're measuring.

And using some of these omics approaches, so you're measuring hundreds and thousands of chemicals rather than individual, you know, 20 or 80 targeted chemicals and just see how it changes after they eat, and then after they've had a period to wash it out. I mean, that will give you some idea of some of the health outcomes or some of the health -- not outcomes per se, but some of the health related issues that are related to consuming those things.

So you might see the increase in some of the good enzymes or increase in production of certain proteins or you may see a decrease in some of the production of proteins or certain enzymes as well. So I think that that's another kind of study that we've looked at. Specifically looking at tea, for example, drinking tea and what kind of chemicals arise and disappear after you drink tea. So that's another type of approach you could use.

MS. HOOVER: Questions?

Dale, up front.

DR. HATTIS: Yeah. George's question highlights the difference between our usual standards of what counts

as good scientific information and what counts as good information for decision making. For science, we -- the hallmarks are validity and reliability. You're measuring what you say you're measuring, and you're measuring a reasonable reproduction, you know, reproducibility and things like that.

For decision making, we want information that is relevant to a choice, that is different across different options we have available, and comprehensive, in the sense that it measures or in some sense differentiates all of the things that we care about across these -- this choice space. And that's hard, but we've got to do our best.

OEHHA ACTING DIRECTOR ALEXEEFF: I'll move over here, so you don't keep turning.

(Laughter.)

DR. HATTIS: And one of the things that I think that we can realize as technical folks is that sometimes -- and I'm going to be advocating this later -- is that -- and you mentioned some birth weight as an intermediate parameter, that is a -- is one of a series of biomarkers, essentially, that is a natural integrator of the influences of -- of lots of different influences, okay.

And so I think we want to have our biomonitoring programs related as well as we can to some of these

natural integrators of effect that we can then relate to health -- rare and hard to measure health outcomes that we care about.

MS. HOOVER: Okay. Any other questions?

Let's see, back there. Someone who we haven't heard from before. Can you identify yourself.

DR. GERONA: Roy Gerona from SFGH, San Francisco General Hospital.

I come from a clinical toxicology background, so when we study say as side effects or toxic effects of drugs, we look at drug metabolizing enzymes. So we have the studies actually that we started where we look at an array of all the snips for particular drugs.

When environmental toxins are small molecules that are also similar to drugs, they have to be transported. They have to be metabolized. They have to be transported to their targets. I was just wondering when I read the literature on environmental toxins, most of the genomic studies are basically studies looking at what particular enzymes or what particular genes are up-regulated or down-regulated. I don't see much study on metabolizing enzymes transporters.

So I was just wondering -- and this is to everyone -- if you have come across particular studies, like say, for example, using -- I know there's a atonatics

dysnema chip that is about 2,000 snips under metabolizing enzymes.

So when you look at the complete picture, right, when you look at say exposure studies, when you look at different mechanisms of toxicities of environmental toxins, has there been groups that are looking at this particular niche, because we're trying to start doing that, and we want to identify people where we can do collaborations with or probably seek advice to study the signs and stuff like that.

DR. BAHADORI: The National Academy of Sciences actually had a meeting that started a lot of this effort to learn from the pharmaceutical side to incorporate metabolism into how we look at the presence and clearance of the small molecules.

Initially, we didn't have good tools to incorporate that into the types of assays that we were looking at, mainly because our assays were sort of off the shelf. We just took what was available, and we didn't really design assays.

So there are now efforts to design relevant assays to incorporate metabolism. Resource is a little bit of an issue, but that's picking up. And there's a lot of intersections between people from the industry who would come from both pharmaceutical and the small

molecules background and they're collaborating. So there's a lot of work, for example, going on down at NIEHS in this area. There's also at NCGC and at EPA, as well industry-related research. So it's just starting.

You know, not having the right environment to do the genomic studies was part of the problem. They're sort of mimicking the pharmaceutical studies, but they weren't really exactly transferrable. So it's just starting to get there.

MS. HOOVER: Okay. Mike Wilson.

DR. WILSON: Hi. Mike Wilson. I'm at UC Berkeley and a member of the Science Panel for the Biomonitoring Program with a number of my colleagues here today.

And as a questions for Dr. Rudel and maybe I'm picking up on Dale Hattis' question that you noted that in the context of the California program that we should consider using the data for other purposes, in addition to sort of tracking and reporting results and levels. And I'm just wondering if you could talk a little more about that.

Thank you.

MS. RUDEL: Well, I guess I'm thinking about trying to use it to tie to help us better understand the relationship between exposure and health effects in humans

by doing some of the studies, looking -- so looking for early effect markers and so on, in addition to just looking for exposure markers. And that that work could be, I think, done most, you know, efficiently and by focusing on the samples that are on people who have high exposures to particular compounds.

So that's -- I think, that's really the main thing. I mean trying to tie it to things that we need to know. We're also -- you know, there's a real need for better ways to measure exposure in some longitudinal health studies, big cohorts, like the National Children's Study. And we're all -- you know, many in the exposure science side of things are aware of the limitations really in just having biological samples.

And so -- but there's a -- I'd say there's just sort of some challenges and lack of information and lack of resources for developing good methods for, you know, okay what is your household exposure for -- you know, what's one measure we can collect one time when we're there that's going to tell us everything we want to know about -- you know, about exposure.

So I think there are some opportunities to develop technology -- you know, some technology development, in terms of -- and that those can be piggy-backed with the Biomonitoring Program.

And I guess another, you know, area is that in -- there are Epi studies -- I'll use -- I'm going to use phthalates as an example. So some of the human studies with looking at phthalates and health outcomes, I'll find -- say there's an association between monoethyl phthalate in urine and health effects that are endocrine related. And since we don't really see many endocrine effects from diethyl phthalate in laboratory studies, you know, questions about what's going on. And I think exploring co-exposures, so DEP is actually really a marker for fragrances. And many fragrances are endocrine disruptors.

And so I think it can help the epidemiologists deal with, what they call, uncontrolled confounding, that basically, you know, they measure one thing. And then there's, you know, 50 or 100 or 1,000 other things that are going to co-vary with it. And we don't know which one is the real McCoy.

MS. HOOVER: One last question here.

Jianwen.

DR. SHE: Jianwen She, CDPH, Biomonitoring Program, Laboratory Leader. And I have actually -- a laboratory, I have a question to Dana. During your talk you mentioned about the realities, like detection limit dynamics, but our collaborator, for example, the

epidemiologist. Not likely you report the data of the change, because we like to compare different studies. So once you provide the different detection limit, do you magically change and then make the interpretation of data more complicated. So how do you give that advice to the people to work with us?

DR. BARR: Everybody likes nice clean numbers. And so it's kind of hard to deal with. What typically I think I would recommend is an average LOD over the study and then just reporting values that are detectable and meet all of your detection criteria below that, because I think that those values, even though they're more variable -- they have more variability associated with it, are better than just imputing values.

I have a hard time with people that just want an LOD, so they can say detect or no detect, because that's setting an arbitrary limit of detection as being your criteria for cutoff for a health endpoint or not having a health endpoint.

So if they have to -- I don't know how to advise you other than to maybe just give an average LOD over the study, and then report everything that is detectable and hopefully that will give you a high enough frequency of detection to deal with. I know it's hard also when you're trying to publish that and trying to describe that to the

editors or to the reviewers.

But the reality is an LOD is just not a static number. And as much as you want to make it, or an epidemiologist may want to make it, or a person interpreting the numbers in some other way wants to make it, it's not. And so you have to recognize that when you're doing your analysis and recognize that there's that variability involved with the analysis.

DR. SHE: And so my second question --

MS. HOOVER: Actually, why don't you follow up after, you know.

DR. SHE: Sure.

MS. HOOVER: So we're going to close here, and we're going to gather again in an hour. So shoot back to be back at actual 1 o'clock. And then we'll start at 1 o'clock that that clock says, which is about 7 minutes late. But try to be back in an hour. And thank you again to the morning speakers.

(Applause.)

AFTERNOON SESSION

DR. ZEISE: If you could take your seats, so we can get started. So good afternoon. Happy Saint Patrick's Day.

And what we're going to do this afternoon is we're going to drill down a little further on this whole issue of comparison values, but also on some broader issues. And we're going to do this as a means of providing some additional context for interpreting biomonitoring results. And in doing that we're going to be picking up on some of the themes that we heard about this morning.

(Thereupon an overhead presentation was presented as follows.)

DR. ZEISE: So let's see here. I'm trying to make one of the themes show up.

Click the mouse.

Oh, okay, I just needed to add a little bit more punch to it.

So this figure is something out of a recent National Research Council Report that shows the progression of exposure to a chemical through metabolism and tissue dose through biologic perturbations and on to health effects. And this morning, we heard from, I think, all of the speakers this whole issue of effect markers,

and the potential for using them to find relationships with biomonitored levels, but also for providing some context. These early effect markers or early indications even from a screen, a genomic screen, for showing some context around biomonitoring results. And we're going to talk about this issue a little bit further this afternoon.

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DR. ZEISE: Okay. So this next figure shows how dose response relationships in an individual are dependent on a number of factors. So if we think about the chemical taken into the body, but there's a whole range of other chemicals that are potentially affecting that disease process. It could be both chemicals taken in from the environment as well as endogenous chemicals. There's also the genetics and the inherent biological susceptibility factors in that individual.

And the chemicals, of course, can be both again endogenous and exogenous. So that determines an individual's dose response relationship. And then there's variability from individual to individual. And that will lead to the overall population dose response relationship. How we think about individuals, how we think about population level effects, and how we think about this paradigm in considering context for biomonitoring results is something we're going to go into in more detail. Some

of the methods we'll be talking about this afternoon take into account these different features and different ways.

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DR. ZEISE: So this final figure shows how the cumulative effects of chemicals on a particular disease process and set of outcomes. And what we are now finding from some of the new science is that you don't have to have a chemical affecting the disease pathway in exactly the same way as other chemicals to still have a cumulative effect on the overall outcome and the overall incidence of disease.

So this again is something really critical as we think about how to translate and interpret different biomonitoring levels in the context of our standard processes for looking at health levels of concern. So that's another issue that we'll be going into in some detail in this afternoon's talks.

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DR. ZEISE: So we have 3 talks this afternoon. And the first speaker will be Dr. Lesa Aylward. And she's a principal at Summit Toxicology. Her expertise is in chemical risk assessment and hazard communication. She specializes in pharmacokinetic approaches to toxicology and translation of reference doses, for example, into biomonitoring levels.

The next speaker will be Dr. Dale Hattis from -- who is a research professor with the George Perkins Marsh Institute at Clark University. And Dale has, for many years, developed and applied methodology to assess health risks. And he's done a lot of work on pharmacokinetic modeling and so forth.

The final speaker is Dr. Amy Kyle. She's on faculty with the School of Public Health at UC Berkeley in Environmental Sciences. She's an investigator with the Superfund Research Program, the Center for Environmental Health Tracking, and the newly established Center on Children's Cancer.

So her research is all about representation and use of scientific knowledge and findings and policy analysis and decision making.

So without further ado, I'll go into the first talk.

Lesa.

I'm going to learn how to work this. Just hit escape?

MS. HOOVER: Yeah.

(Thereupon an overhead presentation was Presented as follows.)

DR. AYLWARD: Lauren, thank you very much for the introduction and the excellent context that you provided

there. That saves some introductory discussion in the presentation.

I really want to thank OEHHA staff for inviting me to come and present at this workshop. I think it's, as other speakers have indicated, that what you're doing here is obviously in the forefront. The fact that you are wrestling with interpretation puts you, I think, miles ahead of some other places and programs that are not doing that. And obviously, that means you're encountering the hard questions first, and it's a big deal.

I have the privilege and, of course, the disadvantage of following 3 really excellent speakers this morning. And one of them in particular, Tina, promised lots of things that I was going to talk about that I didn't know I was going to talk about.

(Laughter.)

DR. AYLWARD: So I'm not sure I'm going to be able to fill all those promises --

DR. BAHADORI: I said you're working on them. I didn't say you're going to talk about it.

(Laughter.)

DR. AYLWARD: So forgive me if I don't get to all of them. But perhaps some of the things we can talk about during the discussion section.

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DR. AYLWARD: What I am going to talk about this morning are -- or this afternoon are some approaches for interpreting biomonitoring data. And, of course, in the context that we're talking about that here, I mean there are different meanings for biomonitoring, but we're really talking about measurements of chemical concentrations in tissues or fluids in people.

I'm going to talk about the concept of biomonitoring equivalents and some background about the development of those, and use of those and give some examples.

And I'm going to talk about some additional work that we're moving towards in terms of additional interpretation resources. These -- the context that we're going to -- that we're working on right now is really in the context of for physicians, but some of the information and approaches will be perhaps more broadly applicable.

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DR. AYLWARD: So when we think about audiences for biomonitoring data and interpretation of biomonitoring data, there really are a continuum of audiences for that. There are people who are involved in chemical risk assessment, risk management, environmental risk assessment. And those people tend to be on a relatively technical end of the scale.

Public health officials may be one step higher in terms of thinking about policy and broader public health impacts. It typically is their focus.

Physicians are another audience. They are increasingly being tasked with thinking about responding to the individual patients, data or patients coming in and talking about environmental data. And that poses challenges for them that we'll talk about a little bit.

Individuals obviously who receive their own biomonitoring data, both as part of your program, the Canadian Health Measures Survey, which is a sort of a Canadian NHANES. They are, in fact, also providing data to participants who request it. I think that's, you know, obviously the way that these sorts of programs are heading, in terms of handing data back to participants if they request it, both because of the ethical considerations and issues that Ruthann talked about, and in terms of just that people want that information.

And finally, the general public who may not be biomonitored themselves, but are obviously very interested in the issues of environmental health and chemical exposures.

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DR. AYLWARD: I've stolen these reasons for conducting population based biomonitoring studies from the

Centers for Disease Control reports. I'm not going to go into all of these, but I'll draw your tension to the last 2 goals and reasons.

Determining the prevalence of people with levels above known toxicity levels, and setting priorities for research on human health effects. And I would submit to you that both of these goals imply or necessitate some sorts of quantitative screening criteria. That without those types of screening criteria, it really isn't possible to do either one of these things in a rational -- a way that's based on using these data in a rational basis.

So I'm going to talk a little bit about some approaches for that.

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DR. AYLWARD: When we think about approaches for deriving quantitative criteria for screening biomonitoring data, there are a variety of approaches that can be used. There's reference range data. These are statistical description of levels in the general population or in a reference population. They do allow you to do things like classify measures as typical or atypical. And Dr. Rudel's presentation, you know, addressed some of the, I think, really valuable things you can get just by understanding if someone has an atypical exposure level.

But it really doesn't provide information on potential health impacts. Either being in the reference range, doesn't tell you that you are or are not having a health impact. And being outside the reference range doesn't tell you if you are or are not having a health impact.

So it really doesn't satisfy the issue of trying to identify levels -- people or the prevalence of people above levels with known health concerns.

On the other end of the spectrum really are the kind of the gold standard. The thing that you'd really like to have are understandings of the exposure response relationship and the terms of the biomonitoring concentrations. You'd like to know what the health impacts are, where they become to be of concern, what the risk in the population might be because of those?

Obviously, that's a really resource intensive undertaking. And at the moment, we have values like that, that are available, but just for a very few chemicals. And we heard talk this morning about -- or yesterday about the CDC guideline for blood lead. And even that value is something that people discuss where that number ought to be. But it's the kind of example of that level. And as I say, it's really available for very few chemicals.

Finally, what I want to talk about today really

is more something kind of intermediate. These are benchmarks that we can derive based on risk assessment methodologies, and some integration of additional data that exists for many chemicals, but really hasn't typically been included in our risk assessment paradigm, which has been focused on external dose.

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DR. AYLWARD: So in these categories, the examples of available screening values, reference ranges. Explicitly, the German Human Biomonitoring Council has established reference ranges based on population biomonitoring data in Germany. So they publish these reference values on a periodic basis.

United States CDC, the NHANES Program, the report can be used to identify the range of typical values in the population in the U.S. It doesn't necessarily cover the populations we might be interested in as, for instance, very young children.

Human biomonitoring response base benchmarks. Again, the German Human Biomonitoring Council has derived values based on principally clinical and occupational toxicology data for a few chemicals, cadmium. Mercury is based on population -- on effects from children, on maternal and infant effects. Thallium, pentachlorophenol. Obviously, the blood lead guideline we discussed. And in

addition, there's occupational guidelines based on the American Conference of Governmental and Industrial Hygienists Biological Exposure Indices and the German Biomonitoring Commission derives values like this as well.

These are obviously targeted at workplace exposures, but they're all the same type of screening values, and they are often based on human biomonitoring response data. So they provide at least some sort of context on those chemicals.

Finally, for risk assessment-based benchmarks, the German Human Biomonitoring Council again has been reacting and deriving these values. And the biomonitoring equivalents that I'm going to talk about a little bit are now available for approximately 80 chemicals. And I'll talk a little bit more about that.

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DR. AYLWARD: Before I get into that, I'd like to talk a little bit about some of the things that you've heard already from speakers today. And what Lauren just talked a little bit about is, you know, evolving risk assessment paradigm. The sort of classical chemical risk assessment paradigm is really focused on a chemical by chemical evaluation with evaluations in terms of external dose response assessment, often based on laboratory toxicology data, really focusing on observable adverse

effects and characterized, I think, by relatively high uncertainty.

We're moving into a space in the risk assessment world, where we're trying to focus more on aggregate and cumulative risk assessments. Aggregate across pathways of exposure. Cumulative in terms of the multiple chemicals affecting a given system or outcome in toxicity.

We're looking at trying to use internal dose-based exposure and response assessment. Increasing focus on subtle biological alterations, rather than gross adverse effects. And finally, population risk evaluations as opposed to bright line evaluations of safe or unsafe exposures.

And then, as Tina described this morning, sort of the vision of where we want to go are really integrated assessments of exposures and factors that affect health and disease outcomes across all life stages, integration of the high technology omics -- the various omics technologies, high throughput screening data, and information about individual genetic susceptibilities to really provide a much more holistic evaluation, including assessment of things like social and community factors that can influence disease development and outcome.

Obviously, as we move down this progression, we're talking about increasing sophistication, but also

increasing data demands, demands for new data, and, you know, increasing difficulty.

Now, what I want to suggest to you is that biomonitoring data, and the BE approach, really are in a bridge in the middle of this continuum. Biomonitoring data really is very powerful in terms of both aggregate and cumulative risk assessment. Exposures to chemicals in biomonitoring data sets can be -- we can look at multiple chemicals in the same individual at the same time. So we really have an opportunity to look at cumulative risk assessment in a way that is very hard to do from an external exposure paradigm basis.

And the BE approach really provides a bridge, a translation from sort of the older risk assessment paradigm into the newer risk assessment and can reflect and incorporate many of the characteristics of the newer paradigm as well.

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DR. AYLWARD: So what I want to do is talk a little bit more about biomonitoring equivalents. And what we consider these to be they're risk assessment-based benchmarks, not health outcome-based benchmarks. And they are, what we consider to be, sort of a practical interim approach as a tool for risk assessors and risk managers principally.

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DR. AYLWARD: So in the existing chemical risk assessment paradigm, and this would be the old school risk assessment paradigm, we're typically working from toxicology data, an external does that we can't -- we don't see any observed adverse effects. Call it a point of departure. And we apply a series of uncertainty factors ranging from 100 to 1,000, sometimes more, sometimes less, to try to derive a quote unquote safe or tolerable human exposure level that's expected to be without risk -- an appreciable risk of adverse effects.

So there's this old school reference dose definition and derivation from UPA. There are parallel sorts of values that derived by other international organizations, tolerable daily intakes, or the ATSDR minimal risk levels. They all have functionally very similar definitions.

And while they are, I think, crude, they do provide some sense in the order of magnitude sort of way of relative potency of chemicals at least based on the assessments and the data available at the time that they were set.

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DR. AYLWARD: So a biomonitoring equivalent is nothing more or less than an estimation of a steady state

concentration of a biomarker that's consistent with those existing exposure guidance values, like reference doses or tolerable daily intakes.

We have available data on pharmacokinetics in humans and animals, also on measured tissue and blood concentrations in animal experiments. We have a variety of data that can be used to make these translations. But fundamentally what they are are translations between a given exposure guidance value. And in this case, I'm illustrating with a reference dose to a biomarker concentration that's broadly consistent in a chronic steady state basis with that reference dose or other exposure guidance value.

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DR. AYLWARD: And the goal of the BE approach is simply to provide a bridge and to leverage the existing data sets and risk assessments in a way that they can be used as one tool in the evaluation of biomonitoring data. Really to provide a translational approach between external and internal dose-based risk assessments.

And the ultimate goal really is to enable the biomonitoring data to be used as an input into risk assessment or risk management evaluations, and perhaps as a tool for prioritization amongst the multiple chemicals and issues that people, who are in a regulatory risk

management, risk assessment environment face. One tool to be used in the context with any number of other tools that they have available.

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DR. AYLWARD: And I'll just say that although most of my discussion and examples here are really focused towards things like reference doses and tolerable daily intakes, that the BE approach really fundamentally is about the pharmacokinetics and about internal to external dose translation. And it can be used with distributional risk metrics. We have examples, numbers of examples, where we've applied it to cancer risk specific doses and evaluation, as well as non-cancer risk evaluations. So it is applicable even into the newer paradigms of risk assessment.

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DR. AYLWARD: I'm dry.

In any undertaking like this, where you're using technical data, risk assessment, risk evaluation pharmacokinetic information, there are a hundred considerations, context, caveats, limitations that really have to be considered.

I'll just reiterate. We really intend and think that these BE values are screening tools for use in a screening level risk assessment context, not bright line

separating safe from unsafe levels. They're derived from a variety of data using a variety of approaches. And they're not any more reliable than the underlying risk assessments or the data that are used to derive them. And in the peer reviewed populations that come along with these derivations, we try very hard to be explicit about the uncertainties and the limitations and the caveats that go with each chemical's values.

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DR. AYLWARD: They're most appropriately applied to population data rather than to the assessment of data for an individual. They're most effective in a prioritization context, where you're looking across chemicals, along with complementary information and assessments. So they're not -- looking at an individual chemical in isolation provides you a little bit of information, provides you much more when you're looking across chemicals. And I'll give some examples.

Biologically transient compounds really present special challenges and we'll talk about that. And there are a lot of additional considerations that are present, both in the general guidelines documents and in the chemical-specific papers.

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DR. AYLWARD: So I promised to talk about

transient biomarkers just briefly. I don't know how well you can see on this screen. This is a really nice set of examples from a recent paper from CDC researchers. These are -- this is a major DEHP metabolite, phthalate metabolite.

These are 3 individuals. Data for 3 individuals. It's the concentration of this metabolite in urinary samples -- every urinary sample collected over the course of a week. There are actually 8 individuals in this study, but I'm just showing 3 here for convenience. And what you can see, as Dr. Bradman mentioned earlier, that you can see that even within a day you see dramatic changes in the urinary concentration within the individuals. We see dramatic differences across days of the week. And we have dramatic -- I don't know if you can see the scales, but really dramatic inter-individuals differences in the actual levels of the metabolites.

And taken together, you know, what these data, I think, tell you is that if you're working in a program where you're taking a single spot sample of a biologically transient compound, you're going to be capturing something that will tell you very little, maybe even about exposures earlier or later that same dame, much less across days or of weeks or months or a life stage or a lifetime.

So I think that this issue of transient

biomarkers and the inter-individual variability of them is probably not sufficiently appreciated and really points to the need to consider the pharmacokinetic characteristics of the chemicals that you're looking at.

Thank you. It's like lunch. You know, potato chips at lunch, just a bad idea.

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DR. AYLWARD: And really contributes, I think, to the observed variability in population biomonitoring data. This is the same metabolite in the NHANES data plotted versus age, in this case. But you can just see the dramatic differences in concentrations between -- amongst these various spot samples. And it turns out when you look across these 8 individuals in this week long study, that the variability that you see in the general population levels in the NHANES program are completely recapitulated by the samples collected in these 8 individuals over the course of a week. You get exactly the same degree of variability.

So what that tells you is that you're doing some temporal -- surrogate of temporal variability in this collection of spot samples across a broad population, which I think is quite interesting and worth a lot more thought, in terms of how we design biomonitoring and interpret biomonitoring for these sorts of transient

compounds.

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DR. AYLWARD: So back to the BE values for a few minutes here. Just a little bit of history. We started this project in 2007. We had funding from a really broad range of stakeholders, Health Canada, the United States Environmental Protection Agency provided funding, the American Chemistry Council and some other trade associations. We had people from CDC and ATSDR, and Health Canada and IUPAC on our steering committee and expert committee.

We brought together people from academia, from government, industry, from NGOs, experts in risk assessment, pharmacokinetics, communication and medical ethics to provide us guidance on the BE concept, on the methods for derivation, the communication aspects of this. The results from the pilot project are available in a special issue of Reg Tox and Pharm.

I'll draw your attention, particularly to the guidelines for communication. I think there's some interesting information in there relative to physicians. We also have some case studies in this issue. And since the workshop in 2007, we've continued work. We've had a 3-year agreement with Health Canada. They've funded development of quite a few more BE values, as well as

other funding sources for that, for BE derivations.

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DR. AYLWARD: And at this point in time, we derived BE values for 80 chemicals roughly. So we're starting -- these are chemicals that are included in various biomonitoring programs. So we've started to approach a point where we can start now to look across chemicals make some evaluations in the context of the existing risk assessments.

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DR. AYLWARD: So I'm going to go through just real quickly just a few examples of the use of the BE values.

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DR. AYLWARD: 2,4-D is an herbicide that has recent U.S. -- very recent U.S. EPA, Office of Pesticide Programs risk assessments. The reference dose is derived from rat data, from a No Observed Effect Level for multiple endpoints, a 1,000-fold uncertainty factor was applied.

The biomonitoring data for the general population tends to range from less than 1 microgram per liter in urine to about 3. And the question is do these levels indicate exposures that are of concern or interest in the context of our risk assessment?

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DR. AYLWARD: This figure is from a paper that Dr. Barr and myself and scientists from EPA and Health Canada published earlier this last year -- or last year, not earlier this year -- where we conducted a review of all the biomonitoring data we could find for 2,4-D, that include occupational and general population. This figure is general population data. It includes both data from the NHANES program, upper 95th percentile, because there were quite a few non-detects in the NHANES, and data from a research effort by Marsha Morgan and colleagues for children and adults in North Carolina and Ohio.

So again this is that range I was talking about from less than 1 to roughly 3 or 4 micrograms per liter in urine. This is the BE value for 2,4-D of 200 micrograms per liter. So now when you look at this -- at these data in this context of the screening value, it gives you information and allowed this conclusion to be drawn, that the current use patterns were likely keeping average exposures to levels well below the current non-cancer guidance value.

So, you know, obviously the reference dose have -- you may have concerns about what that value is, but at least now you have a quantitative basis for looking at the relative exposure levels as reflected in the

biomonitoring data compared to that screening value. And you can make some additional evaluations based on that.

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DR. AYLWARD: You can also use BEs in the risk assessment paradigm that we often use in terms of hazard quotients where we compare an estimated dose to a reference dose. Hazard quotients -- you want the hazard quotient to be less than 1. You might want it to be a lot less than 1. You can compare measured biomarker concentrations to be E values, and use the same kind of assessment.

And so now we can start to compare cross chemicals of the relative levels of exposure compared to their screening values.

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DR. AYLWARD: So, for instance, in NHANES there are over 300 chemicals now that are being biomonitored. And you might want to ask as a risk manager which of these chemicals should I be looking at first? Which ones might be of the greatest interest?

Absolute concentrations tell you one story. They vary by more than a factor of 1,000 across this subset of analytes.

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DR. AYLWARD: But when we look at hazard

quotients, we get quite a different picture. And that might, along with other information, help us in prioritization efforts for either funding research, going out and doing exposure investigations, thinking about exposure interdictions, those kinds of things, based on the biomonitoring data, as well as with other data that you would have available.

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DR. AYLWARD: I mentioned cumulative exposures before. This is an example 4 trihalomethane compounds. These are drinking water disinfection byproducts. They share common toxicity endpoints in laboratory testing, liver toxicity, fatty liver.

And these are the distributions of the hazard quotients calculated from the NHANES data set from '03-'04 for each of the 4 trihalomethane compounds. And this is the cumulative THM hazard index. So on an individual by individual basis, summing the chemical's specific hazard quotients to estimate a hazard index for the trihalomethane exposures.

So now this information can be put into the context of other information about drinking water disinfection byproduct benefits, risks, and considerations of alternatives to feed into a regulatory or risk management decision.

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DR. AYLWARD: Here's an example of the use of BEs in a cancer risk based assessment. So here are the distribution of NHANES values. And these are stratified by presence or absence of organic arsenicals, and different treatments of the limits of detection -- measures below the limits of detection.

But basically, what you can see is that the biomonitoring data suggests that we have a significant prevalence of biomarker concentrations in the range of a 1 in 1,000 cancer risk based on -- this is based on the U.S. EPA Office of Water Assessment from 2001.

And so if you think about the new risk assessment that EPA is proposing, you would bump these all up by about a factor of 7. But nonetheless, it gives you an idea of how to use the BE values and distributional metrics and provide some estimates. And there's some caveats that go along with us.

Urinary inorganic arsenic species are quite transient, and so you end up with variations within individuals. However, this assessment is pretty consistent with external dose-based assessments that we have from other sources.

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DR. AYLWARD: So next steps. I'm running out of

time, so I'm going to go quickly. We really think that the BEs provide a tool that's useful in the risk assessment context, risk assessment, risk managers and potentially public health officials. But we really -- we recognize that a more complete picture is needed for communication with physicians and individuals, that this is by no means an individual friendly sort of tool. We're interested -- obviously, this has been covered before.

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DR. AYLWARD: People are interested in their levels. They want to know how to reduce their exposures, where exposures come from, what health effects might cause, what they should do about it.

And physicians are getting the same questions, but they really don't have reliable resources for this. They generally aren't highly trained in environmental health and risk assessment principles. And the available data that's out there, if they take the time to go look for it, really isn't necessarily appropriate, in depth, focus, detail or coverage for what they need, in terms talking to patients.

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DR. AYLWARD: So we're interested in working on developing a website. We want to include a whole range of biomarker based information, including things like

reference ranges, BE values, clinical and occupational toxicology, epidemiologic information. We want to do it in a reliable reviewed way that's easily accessible. You know, these are sort of huge challenges, but I think there's really a gap out there and a need for this sort of information, including, you know, information where we don't have information, you know, that providing that piece of information.

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DR. AYLWARD: So we're working on planning another workshop for this summer. We're looking to bring together experts in a wide range of fields relevant to this. We're working with John Adgate at the University of Colorado. We've got some seed funding from the American Chemistry Council, but we're really looking towards improving the vision of what these types of information and website might look like, what kind of process we should use for bringing that information together, and identifying potential sponsoring agencies and organizations.

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DR. AYLWARD: So in conclusion, biomonitoring really has become a centerpiece of chemical exposure assessment. We have -- we think that the BEs provide a practical tool that really can increase the value of the

chemical biomarker data, both in terms of prioritization of risk assessment and risk management efforts and to inform resource allocations for the next generation research that Tina has kind of visualized for us. And obviously, we think that additional work remains for developing and providing information for individuals and physicians. So with that, thank you.

(Applause.)

DR. ZEISE: Thanks for a great talk. We now have time for questions.

George.

OEHHA ACTING DIRECTOR ALEXEEFF: Thank you very much for that great talk. I just had -- well, first a quick question and then a statement. So were the original starting values, were they RFDs, U.S. EPA RFDs or Health Canada RFDs?

DR. AYLWARD: Yes. In each of our documents, what we've tried to do is bring together as many national and international values as we could lay our hands on. We did not go to State level values. I recognize that the State of California has values.

In many cases, they can be kind of linearly translated from the other values that have been used. But we kept summary tables of each document that detailed the underlying basis, when those reference doses were derived,

what the data are, et cetera, so that the shortcomings or strengths of those assessments are somewhat transparent.

OEHHA ACTING DIRECTOR ALEXEEFF: Because it reminds me a lot, in the beginning of our addressing air toxics. And when there weren't any air toxic values, other than a few cancer values out there, and we started -- well, one of the first starts was looking at ACGIH values, quickly translating them into public values, and then starting with those. And then, of course, more data came and that kind of stuff. And then you had, you know, better studies and things like that.

And the purpose of that then was to see if there was a level which exceeded the calculated value, and then to look at the sources, apportion the sources, and then depending upon the regulatory capability, to begin to reduce those sources.

So to me I see that could work in this way. I mean, I'm not talking about the individual. I'm talking more about the societal use, where basically one finds these levels. If they exceed that, then let's identify the sources, if one can. So they could be consumer products or it could be air pollution, or it could be something water, maybe. I don't know. Well, arsenic is obviously water -- or could be water.

And then you could go try to address the sources.

So that's, to me, sounds like a very useful, useful product that you --

DR. AYLWARD: Yeah. I didn't emphasize it, but, you know, in our recommendations from our exposure -- our expert panel, they really encouraged us -- you know, when we said well what happens -- what does it mean if you exceed this level, you know, if an individual or a part of your population?

Well, you know, these are risk assessment values. We don't really know what that means, because our risk assessments aren't very good, but -- so they encouraged us to place it in terms of risk assessment follow-up.

So in other words, if you've got a high hazard quotient or something like that, you might want to go back and look and say, ah, you know, is this a reliable risk assessment or is it 30 years old and based on crappy data, and do we know a lot more now? Or, you know, what are the things that go into that risk assessment? And then are there things that -- you know, source apportionment. Do we need to do studies to figure out where the sources are coming from? And then ultimately risk management efforts.

But, yes, that's absolutely the intention is that you need to look more closely. And unfortunately, the bias might be in the other direction. You have a low hazard quotient based on a crappy risk assessment, and you

might be much more interested in that.

And that's, you know, as with any risk assessment undertaking, being aware of the strengths and limitations of your underlying values is really important.

DR. ZEISE: Gina, the last question.

DR. SOLOMON: Only 1. Oh, shoot, I have 3.

This is Gina Solomon. A very thought-provoking talk. Well, of the 3, I guess I'd just like you to talk a little bit more about the sort of individual versus broader population utility of this approach. Because at the end you seemed to be implying that this could be useful for physicians to inform patients.

And then my other question is sort of about the pharmacokinetic models and so forth that you use to underlie all of these extrapolations.

DR. AYLWARD: Okay. So the first question is, again, we typically emphasize this as a population tool rather than an individual tool. But I was talking about with respect to the physician website stuff is trying to provide that context as well as other contexts that might be available for measured biomarker concentrations for a physician to use when he talks to an -- he or she talks to an individual about their results, if they're put in that position.

Recognizing that it doesn't really provide the

type of satisfying information you'd like to have.

Remind me, the second question, I'm sorry.

DR. SOLOMON: Pharmacokinetics.

DR. AYLWARD: Yeah, pharmacokinetics. So obviously I spent too much time just kind of giving you the very high level here. There actually are quite a number of detailed approaches that can be used in this. And they're all detailed in the peer reviewed publication for each individual chemical.

They fall into several categories. We're going to be doing a review article this year with the German Human Biomonitoring Commission members, really talking more about what those approaches are, but they are detailed in our guidelines for derivation and in each individual thing. And they're not all full PBPK models. It's really not necessary in many cases. And we can talk about that off line.

DR. ZEISE: Thank you.

Okay. Our next speaker is Dale Hattis.

(Thereupon an overhead presentation was Presented as follows.)

DR. HATTIS: Well, Lesa, has been properly at pains to emphasize the use of the BE values as a tool to translate the underlying risk assessment summary values that are available in the literature.

And I've been one of the promoters of an insurgency against those original values. So I wanted to -- I said, you know, stress, you know, that there's some reasons for dissatisfaction. As I think she's hinted at as well with the underlying basis of those. But as George, I think, properly suggested, you know, it's a starting point, okay. And there's a couple of catch phrases for innovators in intellectual affairs, as well as the marketplace. And one of the catch phrases is, "If it's worth doing, it's worth overdoing". And the other is, "if it's worth doing, it's worth doing badly".

(Laughter.)

DR. HATTIS: So I think -- but at some point, you want to do it a little better some of the times where you think it might matter to a particular choice.

So I'm going to be emphasizing a couple of problems. First that the risk at the RfD and RfC is -- and therefore at the biological equivalent values is undefined under the usual context of non-cancer assessment.

The second is that biomonitoring is focused exclusively on environmental chemicals will often miss opportunities to discover relationships to early effect biomarkers of public health importance. So I'm going to be suggesting that, in fact, there is an important

opportunity to use -- to leverage the wonderful efforts that you folks are undertaking to, in fact, provide the opportunity to detect things you didn't expect about relationships to ongoing pathological processes that are important in determining the public health of the real human population, and basically that you can -- you don't have to be a prisoner to the animal toxicology, which is, to some extent, sketchy at best.

You can, in fact, give yourself a chance to uncover relationships, at least in a preliminary way, by using these early effect biomarkers that have been -- and I'll talk to you a bit about the opportunities to do that in a number of different biological realms.

And also in that context to address possible program modifications that could help accomplish that, if you, in fact, ever get the resources to do that.

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DR. HATTIS: Then this is just a reminder, some of which Lesa has already gone over, but making the observation that the original 100-fold factor between the No Effect Level and the permitted level layer decomposed into 10-fold for human inter-individual variability and 10-fold for interspecies difference.

That judgment made in a paper published in 1954 was, what we know in the technical term for it, as a SWAG,

a Scientific Wild Ass Guess.

(Laughter.)

DR. HATTIS: And since then, additional factors before been accreted to compensate for the deficiencies in the database. So if you have a LOEL, a Low Effect Level, rather than a No Effect Level, you add a factor. If you have some -- you don't have a full chronic study yet another factor.

The empirical -- the original empirical basis for these factors, if they ever existed, is lost in the mists of time.

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DR. HATTIS: So basically the theme is that the system for defining RfD and RfCs can be improved with our 21st century information and technology.

And just to begin with, it's just hopeless to try to represent the compounding effects of different sources of uncertainty with single factors. And it's even more suspicious that they all happen to be either 10 or the square root of 10. I mean, you know, you would have expected that if it was based on something real, that some of the time you would get something different than the number of our fingers.

(Laughter.)

DR. HATTIS: Using empirically based

distributions allows some, you know, restatement of the RfD goals as the Silver Book that Lauren recommended. Lauren was on the committee that created this new Silver Book, which I think is very welcome. Although, it hasn't -- it's been, well, honored more in the breach than in the observance as of yet.

(Laughter.)

DR. HATTIS: Basically, you know, what we want to try to do if you want to have some consistency in risk management goals is to, in fact, try to define a risk-specific dose. What is the dose of this chemical given my best information that I have, that is likely to achieve, you know, a particular incidence of a particular effect or less, with a particular defined degree of confidence, with a reasonably standardized way of evaluating the uncertainties.

And so this is attainable. This could be done. It's not rocket science, but it's not easy either. So, you know, it's something that requires real effort, but it can be done.

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DR. HATTIS: The current system is based on a universal assumption of population thresholds for non-cancer effects. It's likely to be wrong, both because of accretial human variability, and in susceptibility and

interactions with background pathological processes that are going on in -- that affect the health of the real human population.

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DR. HATTIS: By failing to provide -- and also by failing to provide a basis for deriving some, albeit, highly uncertain finite estimates of risk, the current system doesn't allow development of inputs needed for comparison of potential impacts of different policy options.

George has us -- I really encourage people to do breast feeding or not. Can I encourage use of fish in this lake versus ocean fish? You know, what are, in fact, the trade-offs for real decisions? I can't evaluate that unless I can quantify the risks and the associated uncertainties for multiple sources -- multiple types of concerns.

After considering the fundamental difficulties in RfDs, the difficulties posed by the translation that was outlined by Lesa are relatively minor. There are still problems relating to whether you got the right dosimeter essentially for quantifying the effects. But they're relatively minor compared to all this stuff.

So the from Aylward of biomonitoring is defined as a concentration range. I won't go in this -- the tail.

But basically, I think she's well described, you know, what the objectives are of the Biological Equivalents.

They're intended to be used as a screening tool. They feed into -- most naturally into margin of safety analysis which has been sort of a -- given my heartburn for a long time, because the margin of safety type analyses always begs the issue of which population percentile exactly do you compare with your observed low effect or no effect level from the animal studies.

And, you know -- or your point of departure, you know. So it's not so straightforward as I think the margin of exposure advocates often try to recommend -- or represent

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DR. HATTIS: So the procedure for derivation for phthalates was to identify a point of departure used as the basis for the derivation of the TDI; apply some uncertainty factors, which we've already discussed; estimated total urinary excretion on a molar basis per unit of the parent compound; and apply the urinary excretion factor to the human equivalent POD from step 2. I don't have a whole big problem with most of that, okay. And apply the intraspecies uncertainty factor to derive the BE.

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DR. HATTIS: The difficulties are that the chronic long-term average bioequivalent exposure factor is -- you know, is complicated by, to some extent, acute measurement uncertainty versus uncertainty in the causally relevant does metric. The latter may be particularly important for time-sensitive types exposures. And I'm going to illustrate that later with maybe a pathological example that is the causation of a teratogenic anomaly exencephaly by valproic acid.

Limitations in toxicological testing for the most substances included in biological -- biomonitoring studies. Even when testing is available, there is, you know, often a limitation to a narrow range of ages. For example, cancer bioassays are often started at 6 weeks of age, so you miss the putatively susceptible period for genetically acting toxicants.

And there's, of course, effects of measurement uncertainty spreading observations from the true variability distribution. So basically if I have a real variability among people, and I add some measurement there, that's going to spread the distribution apart from where it really is.

So standard statistical measures of variability, like standard deviations, tend to overestimate real variability. Standard statistical summaries of

uncertainty nearly always tend to understate real uncertainty. And so there's this -- there are these complications that the risk assessors often know about that you were never taught in your biostatistics class.

And, you know, partly for this reason, you know, the recommendation is to not try to use the -- to interpret Biological Equivalents in terms of risks. And I think that's a shame, because I think that's some of the information that -- you know, it's difficult to interpret them, but I think you need to make the effort, at some point, taking into account for specific risks and specific modes of action what the dynamics and uncertainties in measurement and causation are likely to be.

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DR. HATTIS: So here's my pathological example. These are animal data on basically a time dependence of different developmental responses. And the day of gestation is shown on the bottom axis. And you can see that the effects of -- you know, vary enormously depending upon exactly when you give the valproic acid -- this is an anti-epileptic agent -- during gestation, so with the teratogenic anomaly exencephaly being much more sensitive to the exact timing than some of the other measures like field growth retardation.

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DR. HATTIS: This is a curve -- this is essentially -- basically taking -- this is the results of experiments in which the valproic acid was administered in different dosing schemes. These are the pharmacokinetic expectation for a continuous dosing scheme, which is the red line. And if you look at that, a 10 percent effect was produced by about 6,000 AUC units. AUC units are the products of concentration and time.

So in comparison to that, if you give it in 4 equally spaced doses, represented by the blue curves, you get a much better efficiency in terms of production of the exencephaly per unit of the internal dose. And that's, you know, something like 1,300 is the answer -- is the number that you can't read there on that curve.

And if you give it in terms of a single dose that's well timed at the -- at apparently the right time during that, then you can produce the same 10 percent incidence with about a 650 AUC units.

So it matters a lot -- you know, even -- you know, there's a -- the details of exactly, you know, what the right dose metric is can matter -- can give you an order of magnitude difference in efficiency, depending upon your even your internal dose metric that you choose to use.

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DR. HATTIS: So in conclusion, quantitative dynamic theories of toxicants actions are needed for meaningful -- or for the best, anyhow, risk evaluation and quantification. And these theories are not going to be uniform across different modes of actions for different toxicants.

Significant effort is going to be needed to develop appropriate preliminary risk-related interpretations of biomonitoring data. Particularly when you have these time-sensitive actions.

So creative development and testing of risk related hypotheses from the data will generally be needed in order to make good inferences about the sources of the current exposures, and the potential benefits of different options for intervention.

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DR. HATTIS: Current official California biomonitoring goals are, as you see here, determine the baseline levels, establish time trends in the chemicals, and assess the effectiveness of current regulatory programs. But there are 2 possible interpretations of that latter goal.

First, effectiveness in presenting exposures over the current regulatory guidelines. But the second is the effectiveness of the guidelines themselves, and best

protecting or promoting public health. And I want to basically suggest that you can shade your interpretation toward the latter one, if you want to be creative and perhaps best serve the people of California.

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DR. HATTIS: Some useful candidate biomarkers that might be usefully evaluated in relation to biomonitoring exposures include birth weights as a very important initial thing that's -- basically, you don't have to have any cost in measuring this, but it does take a little money to actually go and retrieve birth weights in -- for the women and the pregnant women that happen to be in your study.

But in addition to that, there's gestational age is a good outcome, thyroid hormone levels, and viable sperm counts as other kind of measurements that -- and all of these share the property that they're continuous parameters. They're not, you know, plus-minus variables, but they can be used to predict -- because of their strong epidemiological data that's external to the biomonitoring study, they can be used to make predictions of the effect of changes in these continuous parameters on the rare quantal outcomes of concern, whether our not you get pregnant this month, whether or not you die in the first year of life, that sort of thing that you care about.

In the cardiovascular area, there's a whole set of inflammatory indicators of atherosclerosis. There's also, of course, traditional risk factors, blood pressures. And I'm going to show you some resent findings on blood pressures in relation to PCBs.

There's, of course, heart rate variability. It's a wonderful indicator of status and indicator of short-term stress produced by particles, which I think is a very important kind of a biomarker. And measures of acute damage, the heart specific creatinine kinase that can be used in relation to say carbon monoxide exposures measurable in the blood.

In respiratory issues, you have traditional lung function parameters -- the accumulation of damage that you can measure as FEV1 and FVC. Indicators of pro -- but there's another major kind of indicator, which is indicator of today's progression of something like emphysema, when you find in the urine the products of the destruction of these lung proteins like elastin and the hydroxyproline, which comes from collagen degradation.

For cancer, there's a lot of potential for the use of indicators of somatic mutation. These are likely more difficult and expensive to measure, but they have potential.

For renal disease, there -- kidney disease,

Beta-2 microglobulin is a standard that's been useful in quantifying effects of cadmium.

For neurological, there's a whole big field that is emerging from new brain imaging techniques. Hearing levels after controlling for noise exposure, and measures analogous to the heart-specific creatinine kinase or the -- basically, you'd want to know about today's loss of particular kinds of a neurons if you can find ways of measuring that.

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DR. HATTIS: So the basic idea is that you have some exposure, you have some change in the biomarker of early effects, continuous parameter, the statistics follow. And you use that change to help you predict consequences for the rare quantal effects that you have -- that are more difficult to measure.

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DR. HATTIS: So this is essentially a graph of the relationship between birth weights and infant mortality. And you see it matters a great deal. And it's a crime to summarize birth weight data in terms of above versus below this artificial cut off at 2,500 grams that define -- that the physicians you have developed to define low birth weight. It matters to make a small change one way or another to your odds of dying in the first year of

life. And, you know, and -- the dichotomization of perfectly good continuous data is a mental disease.

(Laughter.)

DR. HATTIS: And it's spread from the physicians, I think, to -- maybe I'm being unfair to the physicians.

(Laughter.)

DR. HATTIS: But to -- anyway, it needs to be combated, you know.

(Laughter.)

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DR. HATTIS: This is the relationship of reported direct cigarette smoking and birth weights. That's the open squares on the one graph, and infant mortality on the other. So you can see both are essentially saturated type dose response functions. They're well described with Michaelis–Menten type functions. And it looks like there's a good chance that one is predictive of the other.

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DR. HATTIS: This is an indicator essentially of birth weights in relation to the incidence many decades later of Type II diabetes.

So the idea is that the developing fetus is not a, sort of, perfectly balanced system with -- you know, with lots of reserve capacity to handle different insults. Essentially what's going on -- what appears like to be

going on is that the developing fetus is making trade-offs in the use of its resources to either make wetwear that's going to be useful many years later, you know, as -- the depredations of age deplete the pancreatic beta cells or not. And that this is -- you know, we need to view that system as subject to not -- you know, not a robust relative to, you know, minor perturbations, but is something that is making the trade-offs it can, making the best use of its resources as it can in the context of different challenges.

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DR. HATTIS: This is new findings, March Environmental Health Perspectives of logs of blood pressures on the Y axis versus PCB levels measured in serum in a recent study. I think that's very -- potentially very important and very interesting. And this is the kind of thing that you could hope to discover, if, in fact, you make measurements of early -- analyze measurements of early biological effect in relation to your biomonitoring levels.

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DR. HATTIS: So exposure -- so okay. I'm not going to go through our recent experience with chlorpyrifos, because I'm running out of time.

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DR. HATTIS: But suffice it to say, that it's complicated to interpret some of it. Even the best blood lead data, when you have rapidly changing exposures, as you do, you know, when the woman goes to -- from her normal environment to the hospital to have a baby.

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DR. HATTIS: Okay, so take home lessons. Biomonitoring measurements have considerable potential to lead to new epidemiological toxicological understanding. They can also be misleading. I mean, there's an old saying on Wall Street that the market has predicted 9 of the last 5 recessions.

(Laughter.)

DR. HATTIS: So cross-sectional epidemiology has the potential to give you things that are not always right, okay.

Obtaining collateral data on early effect biomarkers proximate to the time of biomarker measurements helps you get the most of your data.

Creative mechanism-based modeling is important for interpretation.

And, of course, time and budget constraints are likely to make this even more challenging than it might otherwise be.

(Applause.)

DR. HATTIS: Thank you.

DR. ZEISE: Thank you, Dale. We have five minutes for questions.

Amy.

MS. DUNN: No. No. People raise their hands.

DR. ZEISE: Pardon?

DR. BRADMAN: I think the main thing I want to the say, it will be -- when we have the panel discussion -- when we have the panel discussion, I have lots to talk about.

(Laughter.)

DR. BRADMAN: I guess I'll ask the question though, and this will be for the panel to. As a member of the Scientific Guidance Panel, I'm becoming more and more concerned about how or if, at all, we should be providing some health interpretation to the biomonitoring measurements. It seemed to me the Biomonitoring Equivalents offers the best -- you know, offered the best hope.

But as I look at all the options, I'm beginning to feel that except for compounds like lead or others that are, you know, FDA regulated, have some diagnostic response, that really the best we can do is provide an exposure reference range. And if that's understood in the consent process, you know, I think that's okay. But I

think maybe that's a discussion both within the program and within -- to have between the speakers today. Maybe after the next presentation, we can do that with the Panel.

But it seems to me there's a lot of interesting science here, but I'm not seeing how we can translate that into responding to individual's question of, is it safe?

DR. HATTIS: Well, it takes a lot of work. And I don't say you should not use your Biological Equivalents. I mean, I think that they offer a preliminary benchmark. And as we said, you know, if it's worth doing, it's worth doing badly. But it requires some caveats, I think, to be clear and honest with folks about what you can and can't say with reasonable confidence.

And, you know, and I mean measurements have this appearance of precision. And I think it's hard not to convey this single -- the confidence that it does of a single point value. So I don't know whether you want to try to convey a cloud rather than that, giving some representation of uncertainty about the reference range. Maybe that's better. I don't know.

I mean, that's -- I mean, it would be interesting to have the folks who are doing the social experimentation, you know, think about that as well. I mean, it's nice to have this nice X, you know, but maybe

that's not -- maybe if the reality is a cloud, maybe you can make some other representation of it.

DR. SOLOMON: This is Gina Solomon. Thanks, Dale. That was a fantastic talk. And my question is about that slide in which you proposed looking at markers of effect. And many of the things, maybe I missed some, but most of the ones that I saw were clinical markers of one kind or another.

DR. HATTIS: Yes.

DR. SOLOMON: And so I just wanted to raise the issue of biological markers of effect, which sort of begins to get into some of the ToxCast stuff that was discussed earlier. Some of those types of assays could actually be done on samples from participants or, you know, markers of oxidative stress could be studied. Are you thinking along those lines as well or were you thinking -- because, you know, there might be differences in terms of, you know, the capabilities of a biomonitoring program to look at markers in blood samples, for example, versus doing clinical measurements on patients.

DR. HATTIS: Yeah. My prejudice -- and this is because I'm a risk assessor, okay. My prejudice is to use things that already have pretty good and ideally as closely causal as possible relationships to real quantifiable risks. So whereas, I think that markers of

oxidation are important as causal -- as potentially important causal pathways, they're not yet relatable to my, you know -- I bet you eventually, they're going to be relatable to real incidents in severity of adverse -- of disease processes. But I think we're not -- but today, I wouldn't know exactly how to use a decrease in a glutathion concentration or something of that sort.

But I'm hopeful that eventually that way is open to helping to quantify, you know, risks, but -- in the short term, because I know the relationship between sperm counts and probability of conception, I can quantify that, so I'm happy -- that makes me happy.

DR. ZEISE: Thank you, Dale.

Okay. Our next -- can you save it till the --

DR. MARTY: Yeah, I'll save it.

DR. ZEISE: Okay. So our next speaker is Amy -- Dr. Amy Kyle. And her talk will be understanding and interpreting biomonitoring results in the context of sustainable communities.

(Thereupon an overhead presentation was Presented as follows.)

DR. KYLE: Wow, this is very fancy. Hello, everyone. Well, I'll just tell you right at the outset, I'm the sister from the other planet here today.

(Laughter.)

DR. KYLE: Which is I'm sure why they put me last.

(Laughter.)

DR. KYLE: And, you know, I'm just meditating. This is going to be very obscure to you those of you on the webcast, so I apologize right now. But, you know, here we are in a room, where we have the clock that's wrong.

(Laughter.)

DR. KYLE: And yet we're following it right on the wrong time.

(Laughter.)

DR. KYLE: And I'm wondering just to myself, well, is this because this is the risk assessment community?

(Laughter.)

DR. KYLE: They would rather have a definitive number, even if they know for sure it's wrong.

(Laughter.)

DR. KYLE: So I don't know, but I'm wondering about that.

Anyway, even though -- you know, I -- it didn't say this, I guess, in my bio, but I spent my formative years in public service. And so my interest is really in public policy, and what we do in the real world that

actually might or might not change things for people's health. That's my interest.

And so I think about things just different from a lot of the speakers here. But nonetheless, I found the presentations just fantastic. And I really appreciate them all, even though I'm going -- I may not sound like that, because I'm thinking about this from a different way. So it's not so much maybe that I'm trying to say anyone else's way is wrong, is that I was bringing some diversity into the perspective today. So I hope we can all take it like that.

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DR. KYLE: So what do I do? Yes.

So my -- I have to say this is really cool the thing is down. I can see you. I can see it. It's awesome.

So I'm talking about biomonitoring and then sustainability. And so while that's kind of a big leap, isn't it. So the way I thought I'd approach that is that I want to reflect for a moment on what is this all about? And you know the challenge to the Science Panel is that what it's really about, in policy terms, isn't a scientific thing, right? I mean, why did this law get passed? And why is the money being raised? And, you know, what are we hoping to get out of it? It's not

really a scientific question.

And so when we think about the design of the program, there's a lot of scientific stuff that's relevant, but also what is it about? So I'm wondering about that a little bit, as I hear this discussion. What do we think this is really About?

So I have some pictures just to think, well, does it look more like this or this? I don't know.

And then this issue of numbers and numbers and actions for populations or public spaces versus individuals and private spaces is really on my mind as one way to think about some of what you all are facing. It's not the only way and it doesn't describe everything, but I'm going to say a little bit about that.

And then the third thing is if we're thinking about public policy, then I think it helps to think about environmental health as a policy system, which it isn't completely, but it should be more, but -- and what I mean by that is a system of things that -- a system of actions, analyses, decisions and so on that is collectively, in all its complexity, trying to improve health. And how can we contribute if we think of it that way?

And that's very different from thinking about it from the point of view of science and research. So I'm going to ask you to bear with me for a moment while I try

to explain that. And it leads to wholly different kinds of metrics and different ways of thinking about actions. And I think it gets us back to this issue of unknowns, which I think Gina Solomon was talking about yesterday and how significant really that is at this point.

And then I'm going to say a few words -- and this is probably where I'll cross over, in some of your points of view, into the wacky, which is, well, what do we think about this from the point of view of sustainability, the way some people are starting to talk and think about sustainability. What does that -- how will we think about decision making different? And then how is that different from a risk framing?

Because I think a lot of people here assume that decision making is mediated through a risk framework?

How many people in here think that?

No one will admit it now after the clock, right?

(Laughter.)

DR. KYLE: You know, and I think it has become that. I'm not sure it always was that way. And I don't know that it's serving us well to only think of it that way. And I'm not saying that -- some people hear that as saying, well, you know, Amy hates risk assessment, blah, blah, blah, which isn't completely true, you know. I value the contribution its made. I really do, but I think

maybe it's take -- it's hard and it takes a long time and maybe there's some other ways to think about it.

So that's what my talk is about.

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DR. KYLE: Okay. So these are some pictures. Is this -- my question now, I look at pictures. Oh, they don't show up very well, do they? So this won't be so interesting perhaps.

You can see them, okay. Oh, it's just because I'm sideways.

Okay. Good.

What is this about? What is this Biomonitoring Program about when we think about it? Is it about -- these are pictures I stole from you all.

(Laughter.)

DR. KYLE: So does this capture it? You know, is it about people, individuals, is that what we think about? And obviously, I'm going to make a case, maybe not. But I am starting off with your imagery that I stole out of the presentations from yesterday.

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DR. KYLE: What about that?

You know, those are kinds of products and things that we use in our houses.

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DR. KYLE: Is this what it's about? Are we looking at biomonitoring to understand issues related to combustion in its various forms and markers for that?

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DR. KYLE: You know, is it about dust and stuff in foam and stuff that sort of gets into our houses and lives there forever and is that what we're trying to do something about when we think about biomonitoring?

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DR. KYLE: Is it about packaging and foods and wrappers and containers and stuff that we buy and store things in? Is that what we're trying to deal with.

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DR. KYLE: Or, you know, we have a program in California to deal with cosmetics, to some degree, is that what we're dealing with here?

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DR. KYLE: Or is it about transportation and products and goods and good movement, distribution and all the stuff that goes with that?

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DR. KYLE: Or is it about a lot of these things? You know, is biomonitoring supposed to be about looking at a whole wide variety of environmental factors in someway that makes it more actionable.

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DR. KYLE: Or, you know, is it about thinking about systems? This is a map of goods movement, but are we trying to understand the way things interact with each other and think about that from a health perspective. Goods movement raises a lot of different health related issues, some of which can be informed by biomonitoring. Is that what we want to do?

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DR. KYLE: Or, you know, are we starting to think regionally? This is a nice picture of the region here. There's a lot of work moving us towards regional equity, health. You know, is that a focus that we want to think about when we think about biomonitoring?

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DR. KYLE: And how do we want to think about it? This is a picture that just came out of the new one Bay Area sustainability initiative. And the details aren't important, but the point is that they're setting targets that have to do with health. And they're looking at strategies and doing modeling to try to figure out how to achieve those.

Now, is that a way? You know -- and again, this is in the context of climate change and regional sustainability. And a lot of people are involved in this

who want different things and there's a lot of discussion and negotiation going on about how this will turn out. And this is a first draft of one piece of that.

But is this a way to think about biomonitoring and what it might tell us?

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DR. KYLE: Now, this is the second half, which I'm just going to skip.

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DR. KYLE: And if we were to think about biomonitoring and, you know, have sort of a list Of where we are now and where we're trying to go, you know, in policy terms, can we think about biomonitoring that way? That's what this is. This is a sustainable community strategy planning process, with some of the inputs and outputs and steps and metrics. And they're not using biomonitoring, at this point, but they're talking about things that could be biomonitored, at least in part.

And they're talking about equity and cumulative impacts and stuff like that. So again, where we're talking about biomonitoring, what are we really thinking about?

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DR. KYLE: Another example. This is from the Environmental Health Coalition in San Diego. And this is

just one of their brochures about what they're about. And, you know, they're talking about issues in a community. And the accumulation of burdens that they face. And you can see that in the pictures and also in the words. And they're working to reduce pollution, protect health. You know, is there a role here? Is this kind of a way of framing what we're thinking about in biomonitoring?

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DR. KYLE: Or again, are we thinking about individuals? You know, I don't know. I think there are a lot of choices to be made, but I guess my point is maybe a little more discussion like that would help just to recalibrate what has been done. And, you know, I think we've come a very long way. So I think if this is maybe in the next phase, and the future of this as it continues to evolve.

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DR. KYLE: Okay. And this issue of individuals and the role that the Biomonitoring Program should play in trying to predict health related issues for individuals. You know, I think it's really -- this is really an issue that bears some thought. And the more I think about it, the more I think that this individual's sphere is a troubling one for the State program for a State -- any

State program that's supposed to be about protecting public health and policy action and so on to get into.

And I see why. I mean, it's an intimate thing to biomonitor someone, right? You know, it takes something that was part of a living being and measure it and give results back. I mean, that's an intimate thing to do. And you have an intimate sort of human reaction to that to want to give that the right meaning.

But there are just real differences, you know, between what we say in a public sphere and in a population basis than what seems appropriate for an individual. And, you know, I think -- I really have -- the more I've thought about this in developing this talk, I think the State's responsibility is to the public. And maybe, you know, Asa just said something about the notification and the initial framing of this for the participants. I mean, maybe it just should be framed as being about that, and set aside some of these issues for individuals.

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DR. KYLE: So you know I have a couple of tangible things that have been on my mind. One is that our record for advice is so bad, you know. I mean, I'm sure you've seen this slide before, the advice on lead over the years. You know, we used to say, well, we'll worry if it was over 60. And then when I was a kid it

went down to 30. And then it went down to 25. And now we're saying 10, but we don't really believe it.

(Laughter.)

DR. KYLE: Right? Nobody thinks 10 is a safe level anymore. And they even rate it down. They say, well should we change it to five? We know there's effects at five. And so here's the gold standard for giving advice and our advice is always wrong. And so, I mean, I just have a lot of humility about -- and, of course, I'm not a medical doctor. So I don't do this anyway. I give people my opinion, but, you know, it's just as a whoever.

But I mean how much can we think that we can offer guidance to any individual on their health based on what we know?

I don't think very much. So I just wonder about whether we should be thinking about that just completely differently.

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DR. KYLE: And one other issue to comment on is the question that Dr. Hattis raised about these point estimates and dividing lines, and whether that's even the right way to think about health and trying to promote health. And these are -- this is an example again from -- related to the work on lead that talks about moving -- what happens if you lose five points in IQ across a whole

population?

And what this graph is trying to show is that you move a bunch of people who were in a normally functioning range into a retarded mentally retarded range, as that's defined by people who define these things. And you move a bunch of people who were in a gifted range out of that. And so it's not only about the people who, you know, are right above and below some dividing line. You're moving a whole population on a distribution.

And we see this now in some of the interventions on things like salt. You know, should we only try to deal with the high salt people or should we just have a low salt message. And the thinking of public health community is it will help everyone if we say let's all try to reduce salt in our diet and get it out of processed foods, et cetera.

Move everyone down the distribution, rather than target the people who are right at that supposed dividing line between too much and too little.

So, you know, it's another component to this kind of advice that I wanted to just to raise in a different way, I think, than you had raised basically the same thing.

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DR. KYLE: I think I'm just going to skip that

for now.

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DR. KYLE: And one last -- this is probably a politically incorrect thing to raise, and I recognize that. But one other thing that's really on my mind, as I think about this discussion, is there's so much political opposition to setting reference doses and health standards. And, you know, people's appointments get held up, and agencies getting threatened with being abolished. You know, and I mean, there's just -- it's not like its -- everyone goes into a room and it's a friendly little thing. It's a very deeply contested process. And so our health protective levels are the result of a lot of political negotiation as well. You know, I think we all know that.

But if we're really going to try to rely on this more, then don't we have to -- can't we do something about that? I mean, shouldn't we be trying to buttress up the level of competence of those and reduce the politics, if we're going to try to move in that direction.

I guess it just worries me. We're talking about the limitations of model -- of the modeling and so on, but maybe not about the overall decision making process. I mean, I would have ethical concerns in using them in a way, because of that.

IRIS, you know, which is EPA's system for the reference doses is described as failing by the Government Accountability Office, because they can't get stuff done. You know, some of these things have been in review since I was in grade school

(Laughter.)

DR. KYLE: So you know, there's more of a systematic problem here that I think we need to recognize as a community, if we're going to be talking about this.

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DR. KYLE: Okay. So to moving on to public health a little bit as a system, moving on to this next thing. The purview of environmental health traditionally has been things like this, pollution spewing them out of facilities, all those kinds of things.

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DR. KYLE: And we keep bringing in new things. You know, we have indoor environments. We have these new agricultural things. We have climate change. We have consumer products, which I don't have pictured, but I had before. And I think one reason that biomonitoring has become so central is because a lot of these things aren't in our I -- in what monitoring systems we have. And so biomonitorings become kind of a stopgap way of seeing what's going on. So, you know, the phthalate results and

maybe even the BPA results that were so shocking really at how much exposure is. It's somewhat of a metric of what's missing out of the system as a whole.

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DR. KYLE: We're moving also towards a broader understanding of the significance of contaminants in environmental health. I think George brought up this idea of cumulative impacts of multiple factors and other stressors. There's a lot more work on social determinants, sensitive windows for exposures, the importance of background levels of things, and the variability of sensitivity and response that people have talked about here.

So we are recognizing that more things matter and that the ways that they matter are maybe more complicated than many of our methods would reflect.

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DR. KYLE: And I just -- I wanted to for a moment note that in the biomonitoring program, there's a discussion of the significance of honoring the principles of environmental justice and the environmental justice plan for the state. So it's recognized even in the statute in this way, that some of these other issues need to be contemplated as part of this.

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DR. KYLE: So, you know, if we think of a system where we're trying to look at what the functions of environmental health should be and how they relate to each other, rather than starting from the data, you know, rather than starting from biomonitoring data, you know, I've put down some categories here of things that we do in environmental health. You know, we obtain data. We try to analyze it and understanding things. We communicate to people, so they can understand. We try to take effective actions, and then evaluate to improve and correct.

And it's very complicated, because it's not located in any institution. And I don't know if you've ever seen Tom Burke's pictures of the environmental health system, but they're like these mazes, you know, of different people who are involved.

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DR. KYLE: And this is a simplistic diagram that tries to illustrate this in an oversimplified way using a little bit of the World Health Organization framework for this that looks at driving forces and sources of agents, and ambient media, and then exposure media and then finally people down the left-hand side.

And my whole point in showing you this is that when we think of this as a system, there are ways of intervening at each of these different stages, you know,

that we have policies that are at the very more upstream end. Then we have policies at the very downstream end.

Now, biomonitoring is, in some ways, almost beyond the downstream end. It's sort of after we've failed, you know, we have contamination in people. And our interventions, our public health interventions, should be before we get to that point.

So how do we think about biomonitoring in this context, I think, is -- you know, where could this be useful, helpful, advance us? And I have some examples here that, you know, I don't have time to go over in detail that are the arrows about where biomonitoring results and data have been used in these -- at this different levels.

So, you know, I encourage us to think a little bit more like that.

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DR. KYLE: This is a better more complicated example of the model that I'm not going to go over.

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DR. KYLE: So in doing that, then, you know, I have some suggestions in terms of the kinds of metrics that we've talked about.

So far we've talked about these equivalents for single chemicals, you know, the equivalents between our

reference doses and what that would mean in biomonitoring terms. And that's single chemicals. So I guess that's all to say about that.

And I think there's other kinds of metrics that would inform us at more of a systems level. And one of them I call group scale metrics, which is occurrence metrics. And this comes out of biomonitoring, what is present and where? You know, what are time trends? Are things getting better or worse? What about metrics of burden that could look at this issue of variability, but in terms of overall burden, not only just individual pollutants? And what about burden metrics that combine with other stressors? You know as we try to think about other determinants, are there some ways that we can look at that overall burden?

Who's giving time here?

Have you given me a signal yet?

DR. McNEEL: Yes, I gave you that one.

DR. KYLE: Okay, I didn't see it. I was wondering. I thought, hmm, I haven't seen anything here.

(Laughter.)

DR. KYLE: The second one -- I thought well, maybe I'm getting a free pass.

(Laughter.)

DR. KYLE: Okay. Geographic metrics is another

one. And then there's system scale metrics. And maybe this is even a little bit wackier idea. But, I mean, we talk about people's anxiety when they get their biomonitoring data, and, you know, whether having that data causes them to worry.

But what's the -- you know, maybe not having that data is a problem too. You know, I mean maybe there's some ways we could be talking about, well, how much of what we should know do we know?

You know, I mean, what percentage of chemicals in use are represented here or how much of the exposure that we have, do we understand in any way, or, you know, where are we in terms of how much -- how far along in terms of what we think we need to know to interpret something?

So we have some kind of performance metrics that are outside simply the cause and effect, but help people to understand where we are and where we have to go.

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DR. KYLE: And then this issue of the unknowns. You know, I think metrics for the unknowns are really important, and hard to do obviously. But we're so lacking in any ability to describe what we haven't gotten to or what we haven't been able to do.

And, you know, I think we need to begin to have a way to talk about that, again to think about this as a

system. You know, what percent of the exogenous compounds did we measure when we did this or what percentage, even in the environmental compartments releases do we monitor, account for? You know, what is our system really doing?

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DR. KYLE: Inequality metrics is something we've done a little bit of work on, not related directly to biomonitoring, but again how do we measure inequality is an important thing in some of these contexts?

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DR. KYLE: Okay. And then cumulative impacts. I've talked about this -- mentioned this already. And I'll just remind us that OEHHA has a draft of an approach to begin to work on cumulative impacts.

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DR. KYLE: All right. So sustainability. This is, I guess, my last sort of perhaps wacky step here of different ways of thinking about how to move forward in environment and health and solely risk-based sorts of approaches. And the sustainability people -- this is in the context of climate change, but what they're -- and I've quoted this from a paper by McMichael et al. talking about thinking of the larger trajectory of what we're facing in a larger way.

And we are seeing a move towards sustainability

in a lot of different contexts. And I think to capture maybe the gist of what that represents is a sense of trying to at least be moving in the right direction on things. You know, at least if we're going to try to move towards a more sustainable world, we want to stop having things get worse and having them start to get better. And so time trends sorts of analyses are important in looking at this.

And it's something that you can understand in a much more simple way, and that doesn't require the level of kind of argument and debate and discussion and endless kind of reworking that we've seen in this kind of risk assessment world. So I'm not saying we should abolish risk assessment, of course. And sometimes you need the level of the bright line number that you get out of that for some purposes.

But I'm also wondering whether it might not be time to look at some of these metrics that look at whether we're moving in the right direction, and sort of softer measures of can we get rid of some of the exposure that we have? I mean, we have perhaps, what I might call, gratuitous exposure in toxicity, I think, in some of the products, where we don't really need to have the exposure. We don't need to have the toxic substance. Maybe we can think of ways to measure that and move toward that.

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DR. KYLE: So there are a number of models that have been developed --

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DR. KYLE: -- that articulate part of this. I think another component of it though, and I'll just cut to my last slide here --

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DR. KYLE: -- is that it does require engagement with people at a human scale. And so how we can incorporate our kind of way of thinking about biomonitoring, that things that are happening at community and regional scales is one part of what I think will help -- would help us think about biomonitoring in the context of sustainable communities.

So just to sum that, you know, this is about public health actions and public venues. It's part of a system that's oriented towards trying to improve health across these various ways of acting. It connects to a larger movement. It has to do with human scale and focusing on resilience and building that. And I think it has to allow for aspirations for improvement and not discount that as unscientific or not relevant to what we're trying to do.

So I thank you for your attention. I'm sorry I

went over a minute or two and I look forward to the discussion.

(Applause.)

DR. ZEISE: We'll take a couple questions.

DR. KYLE: I know what time is it, right?

DR. ZEISE: Ruthann.

MS. RUDEL: Hi. Thank you for that talk. You helped me tap into my inner anti-risk assessment child.

(Laughter.)

MS. RUDEL: And it just -- I'll just underscore, you know, underscore some of your points by reflecting on a meeting that I was at awhile back --

(Thereupon cell phones rang.)

MS. RUDEL: Everybody is getting phone calls.

(Laughter.)

DR. KYLE: Another nuclear site must have blown up or something.

MS. RUDEL: And we were talking, I think, about PCBs or mercury, but something where we do have a pretty good idea of what the health effects are, and that they are occurring at current exposure levels in the general population, and even sometimes what the sources are or how to intervene.

And somebody got up and said, you know, what really is the point of doing more environmental health

research to understand the relationships between exposure and disease if even when we do know the answers we don't really do anything about it?

So, yeah, I don't know how the Program can move us to the direction of actually, you know, acting on the information that we have. But I wouldn't -- you know, hope it can.

DR. ZEISE: Melanie.

DR. MARTY: Yeah. I just had a comment. This is Melanie Marty from OEHHA. Sorry.

Amy, I really liked your presentation. And I do risk assessment and I'm proud of it.

(Laughter.)

DR. MARTY: And, yes, I understand -- we all understand the uncertainty. And the reason for the uncertainty is the complete failure of chemicals management in our society. So it just pervades everything. It's why we're even sitting here.

But I think you have made some good points that may be, you know, Asa may have been -- and I'm interpolating what he was saying. But it's so hard to take individual measurements and tell anybody anything about what they mean. But I think that overall the biomonitoring information is really useful for exactly what you're talking about.

Information is power. Somebody said that earlier. So it will feed into -- you know, never underestimate the power of market or people's choices. If they -- if the public starts to realize these things are everywhere and in all of us, I think we will see a much faster shift in exposure reduction on the part of people making products than any other regulatory hammer could do.

DR. KYLE: Well, I think these are maybe a little bit more in the phrase of comments than questions. But, yeah, you know, I think you're absolutely right. So maybe just leave it at that.

DR. SOLOMON: Okay.

DR. ZEISE: Well, now what we do, I think what we'll do is have a discussion of these last 3 talks, and then take a break, and then have all the speakers come up. So I was wondering if the 3 speakers could come up to the front. And maybe we could start with you commenting on each other's presentations and having a little discussion, and then we'll move it out to the audience.

MS. HOOVER: Just clarify that we're switching the agenda.

DR. ZEISE: Yes. We're switching the agenda. So we're going to have a discussion of this. Then we'll take a -- we're going to have a discussion of this afternoon's talks. Then we're going to take a brief break, maybe 15

minutes, and then we'll have all the speakers come up and have a discussion of the whole day.

So, Dale, would you like to start.

DR. HATTIS: Well, I guess I want to respond, to some extent, by saying that bad as the numbers we can make are, and, you know, I think helping people understand them as best we can is empowering. And we should affirm the autonomy of people as you, I think, indicated. And that's part of our -- that's part of our duty as techies to destroy our special status as custodians of this information by, in fact, communicating what we think we understand as best we can.

DR. ZEISE: All right.

DR. AYLWARD: Yeah. I mean, I have just a couple of observations. I think that the systems level approach and thinking process that you've -- and the questions that you've outlined, Amy, are excellent ones. And I think they really are the central way to really put these things all into a framework as we think about environmental health and sustainability. And I completely -- although the spaghetti charts and the process and these kinds of things tend to be off-putting, I think they're really important to think about the interactions in the system. And I think that that kind of thinking is really important.

As Dale says, I'm probably more of a techie, and so I try to use my skills on the technical level. But I recognize, and I think it's incredibly important, to have the thinking going on at a more meta level to really think about these things.

And, you know, I was struck by many aspects of Dale's presentation. I don't disagree with Dale at all about these things. And I would just suggest that many of the limitations he identified in the approaches that we've outlined really are the limitations in the underlying risk assessments not specifically in the types of things that we're trying to do with those by integrating other data.

And then finally, the other observation is that I want to go back to the streetlight and spot -- and flashbulb metaphors that people were using this morning. And I think it pertains to Melanie's comment, in terms of, yes, people absolutely, when publicity and information about exposures come out and people absolutely, both manufacturers and people who use products, they do tend to reduce their use. They reduce the thing that's getting the attention today, you know, whatever that happens to be.

My concern always is we have something that's extremely well studied, and we understand risks and the uses of it. And we abolish it, because it receives

attention and it gets replaced with something else. And that something else is almost never understood or studied or evaluated anywhere near to the degree that the thing that we're replacing is.

And so then we're constantly chasing this, because now we're not biomonitoring that chemical, not this decade, maybe next decade. And so I really think it goes back to sort of this more systems approach, where we really need to think about the fundamental characteristics of what we're doing in a way that allows us to sort of avoid chasing the last emergency, which got the attention, and moving towards something that just fundamentally makes more sense.

DR. HATTIS: Yeah. I absolutely agree with that.

DR. KYLE: I think it's my turn.

(Laughter.)

DR. KYLE: So I absolutely agree with that, too.

(Laughter.)

DR. KYLE: Sorry, Dale.

DR. HATTIS: That's okay.

DR. KYLE: You know, yeah, absolutely. And commenting -- just to comment a little bit on some of what you presented. I really liked the way you showed that, sort of, transition in methods. And, you know, the evolution of -- I think you might have called it risk

assessment.

But what you were talking about is our evolution from single chemicals to looking at cumulative impacts and then this -- so we have conceptual evolution. We also have a methodological evolution happening with all this new stuff about high throughput methods, and so on. And so I think we really have 2 transitions going on. We have this testing transition that is really getting pushed hard now by EPA and NIEHS for a variety of reasons.

And then we have this evolution of thinking too, and -- you know, that that -- so one of the issues that raises for all of us is what are we going to turn our attention to? Because you can't pay attention to everything. And so your time and attention is maybe the most limiting thing that we have. And so how can we marshal our resources and time and attention in a way that takes advantage of all the wonderful wealth of knowledge of all the speakers and your worlds and friends and everything, which I completely honor, not really being a risk assessor or, you know, any of those things.

But also connect with the next phase, sort of, on the policy side too, you know, bring these things along together. And that's to me where there's maybe an area of just collaboration that's bigger than just being about the risk assessment community.

DR. HATTIS: Yeah. I just wanted to continue. You know, experience, which I've accumulated now in excessive amounts, is the ability to recognize a mistake when you make it again. And Lesa's general statement that, you know, you eliminate hazard A and it gets replaced with closely allied chemical B, this has happened quite a bit. You know, I mean, I remember there was during Vietnam War there was quite a hullabaloo about Agent Orange and 2,4,5-Trichlorophenoxyacetic Acid.

And after the hullabaloo and the immediate emergency response to the teratogenic information on that chemical was understood, it was replaced in people's lawns and gardens by Sylvex, which as it happens is (2,4,5-trichlorophenoxy) Propionic Acid.

Well, was there good reason to believe that was better? I suspect not. But such was the chemical-by-chemical focus of the regulatory decision making, that that's what happened. And, you know, maybe it's -- I mean, I don't know, in the fullest of time, maybe it turns out that that was a wonderful idea, but I'm not sure.

And to some extent, you know, I get afraid that we, you know, tend to be -- you know, as contributors to decision making, we tend to be doing this more symbolic kabuki charade, rather than making real improvements. And

so I think it's trying to do the system's thinking is hard, just because it's hard to develop comprehensive information about the relevant choices.

But if we understand that trying to understand the different pathways, the different trade-offs of different kinds of effects, that that's the real problem, that rather than a single pathway, single chemical, single effect type analysis, you know, that's important. And somehow we have to help the people who are making the frame -- the legal framework accommodate the real limitations of our -- of the information that we can produce, and still allow reasonable choices to be made.

DR. ZEISE: Okay. Anyone, either Amy or Lesa like to comment or should we move to the audience now?

Okay. Mike.

DR. WILSON: Sure. I'm Mike Wilson at UC Berkeley. That was just a real interesting set of presentations. Thank you. And I guess I'm sort of picking up on Amy's theme about systems thinking. And that the system of environmental health has been about gathering, analyzing information, interpreting that information, communicating it and then perhaps setting safe levels and so forth. And you've offered this critique of that.

And one of the things that struck me as I was

hearing the talks is that this kind of discussion never occurs in the arena of the people that are designing the chemistries that we're trying to work with -- set risk levels for and so forth.

And so I guess -- I guess my -- I have a question to you. And that is that is the problem really about risk or is it really a design problem? And that can -- by a sort of chemical design problem, and are there characteristics of the substances that we're finding that are biopersistent and so forth that are problems of chemical design. And is there a role that the environmental health sciences can play in assessing that information from a design perspective and communicating that to the world of chemistry and chemical designers?

DR. HATTIS: I could respond a bit. I think the answer is tentatively yes, there's a tendency to be fighting the lasts war, of course. But we have enough experience to recognize certain flags, let's say. So if you showed me a chemical that has an aliphatic -- that has an aromatic bromine in it. Okay, I'm going to say, wow, I've seen that kind of a grouping before. That tends to be persistent in the environment.

If you showed me an aliphatic bromine, that's a straight chain, you know, that tends to give -- make an alkylating agent. So I'm going to worry about that. You

show me a chemical -- but I don't know enough to be really good about trading that off against, say, an aliphatic double bond, right. I know that a double bond sometimes gives rise to an epoxide when metabolized. So I now know enough to recognize those things, and -- but I think we need to develop the, you know, quantitative system -- you know, structure activity understanding to a greater degree than we now have, I think, in order to give the chemical designer good clues as to how -- but so, again, when you're saying -- I mean, we want to be as green as possible rather than green chemistry.

So, I mean, I think -- so, I mean, basically if you say I see an ester linkage, ah-ha, well, this I know biological systems handle pretty well and is going to be relatively short lived, other things being equal. So that's a good grouping in some sense. So it's nice -- it has -- so this is drawing upon my 40-year old understanding of -- of organic chemistry. But I think that there is some lessons we can draw.

But you'd show me n-hexane, right. If I didn't know that that was metabolized to a neurotoxin -- a neurotoxic metabolite that is hexanedione, I would be hard put to figure that out.

So I now know how to recognize -- you guys are more -- you're more chemical perhaps than I am.

DR. AYLWARD: And I mean there's this fundamental problem too, in that a lot of the design characteristics that make a chemical commercially valuable, you know, really stable, flame retardant -- you know, a lot of these things that actually they're really good for a purpose, you know, protecting wires or doing things, being in a transformer. And they're the exact same things that make them environmentally undesirable.

I mean, there's some fundamental issues with that. Reactivity, you know, may be very desirable from the point of view of the chemical manufacturing process. The chemical that's going to get used in may be very undesirable from the point of view of alkylating a DNA, you know, strand.

So, you know, and the problem I think is like many other parts of our society is that, you know, it used to be that big chemical companies that were coming up with new chemistry and new things, they had -- they did have toxicology departments. They had things -- you know, people who at least had some thinking on these sorts of things and they could do something if they were asked.

Now-a-days, you know, there are only a very small handful of chemical companies that have any kind of toxicology or health people involved. And they're often not involved in the design process. They're involved in

reacting to other issues that have come up post-market.

And so I think that it's -- you know, it's just like a lot of other things is that we've cut things and don't have an integrated system on that side. So I think there are characteristics that could be evaluated, but I also think that this is an arena where maybe some of the high throughput screening omics and some of these things might actually help us a lot. Because as Dale says, you know, there are some things that you might consider to be a red flag, but, you know, things come up all the time that we look at and just say, you know, ooh, that turns out to be really bad. We don't know that.

I mean, I think phthalates. You know, you've got your ester linkage and you say oh, that should be good. It breaks down. It's like, well, it turns out it happens to work really well at being an anti-androgen, you know. And so I think that there are -- I think it's very hard, from just a pure chemical design point of view, to anticipate all those things.

Maybe these screening types of technologies will help us recognize pathway perturbations that are of interest. They have to be more metabolically robust. It's one of my biggest issues with this high throughput screening and omics technologies right now is that they, in general, don't include metabolic activation systems

that are relevant. Some of them have a partial system involved. But, in general, that's not the case. And so unless you're testing the relevant, you know, approximate metabolite that actually is going to be toxic, you may miss it completely or you may miss a detoxification pathway that's, you know, extremely efficient. And you, know, you might argue that's a better error to make.

But nonetheless, these system are really not capable, in that sense at this point in time. And I continue to have reservations about it from that point of view.

DR. HATTIS: Yeah, my own --

DR. KYLE: A brief comment. And that is, you know, we're running into this world with these new methods. We're going to have methods that can screen stuff out, in the sense of finding things that are problematic, but not really confirm that they're safe, right, because these high throughput methods are going to be able to find problematic mechanisms. So some of -- but they are testing narrowly, so we're not really sure that we're not missing everything.

So, you know, I think this is an issue we need to think about sort of in a policy framework. But with regard to the design, well, they still test pharmaceuticals, right. And they design those from the

ground up. And so, you know, I'm not really that optimistic it can be -- it seems like there's, of course, a role for design. But if they haven't solved that with all the work that's been done on pharmaceuticals, it seems very unlikely that you're going to somehow differently solve it all for chemicals. So, you know, I would imagine there's going to be a role always for both, and then even for the population follow-up as well.

DR. PARK: Yes. June Soo Park from the California EPA.

Yes, you know, this is to Dr. Wilson. I'm a lab person so hopefully I'm not in the wrong territory. So I can speak only lab language. You know, as we talked about the -- how good our data is, you know, that we have certain procedures, QA/QC. You know, we have several -- also we cross check among the laboratories to, you know, produce some quality of -- good quality of data.

Whenever I'm in the biomonitoring talk or session, I feel, you know, strongly how important data interpretation is. You know, the lab person only know chemical is there, and the level is high or low. But the data interpretation will kind of talk on PF of us.

So my question is to our California Biomonitoring Program. My first question is for the risk assessment. Do you have some standardization of risk assessment? I

run the -- you talk about the birth weight effect, but I know that there has been long time controls there I believe.

So I think putting some barriers -- so taking out the barriers will give you a very different result. So my question is kind of leap of a way to approach the data for the California Biomonitoring Program. Do we need some standard risk assessment method, like a check point. Many barriers should be there, like our QA/QC can tell quality of our data for the statistical analysis. Do we need that kind of approaches in our California Biomonitoring Program?

DR. HATTIS: The effort to standardize risk assessments has been a goal since the early 1980s. And I think has done, as a general matter, more damage to the field than not, even though it has -- there have been notable efforts led -- some led by Lauren, that produce really useful results in the short run, but it also -- it has the effect of telling people that if you do -- if you go through these things, these, you know, semi-mechanical steps, you will get to a consistent result.

And the problem is that you give -- you can achieve procedural consistency much more readily than you can achieve consistency in the goal, given different, you know, kinds of circumstances posed by different chemicals,

different modes of action and different endpoints of effect.

So I think that while -- you know, as I said earlier, if it's worth doing, it's worth doing badly, and it's worth doing quickly in standardized ways. It's also worth transcending your -- and telling the assessors and the managers that it's worth the candle to try to critically evaluate the way you've done things in the past, and to calibrate your quick standardized procedures against some, you know, more elaborate procedures.

Usually, the standardized procedures are made rapid and easy to do, but are never calibrated against the risk goals that you're trying to achieve.

DR. ZEISE: Yeah, I think we're all for transcendence here. And I think what we'll do -- and I agree, I think this issue of risk assessment though opens up all kinds of feelings and ideas. So I think we'll bring it back now to kind of the more biomonitoring kinds of questions with, Melanie.

DR. MARTY: Yeah. Good, Lauren, you read my mind. You know I had a biomonitoring question.

It's actually for Lesa. In terms of the Biomonitoring Equivalents that you calculated with the method. I apologize because I have not read the papers. But within the pharmacokinetics analysis, are all of your

inputs -- are they distributions and do those equivalents account for a difference in it by age?

DR. AYLWARD: So let me just talk really briefly about this. This is something we could talk about maybe off-line too. But we have a couple of different -- about 4 different approaches that we've typically used in this. And it's dictated by what data are available.

I'll give you a couple of the elegant results, or elegant approaches. So for triclosan, for example, in the chronic bioassays that have been used as the basis of most of the risk assessments, the experimentalists measured serum concentrations of triclosan throughout the courses of -- repeated measures throughout the course of the bioassays. So it's a chronic bioassay.

So you have actually for the no effect group, the low effect group, the biochemical changes, you have relatively robust measurements of the serum concentrations of triclosan that were present in those animals.

So now you can imagine if that -- you know, if that average level is 21, you know, milligrams per liter. I don't remember off the top of my head what it was in the No Effect Level group, and you're going to go and think about your risk assessment, and on an external dose basis, we divided by a factor of 100. Well, if you divide by a factor of 100 from that internal serum concentration, and

then you go biomonitor serum triclosan and you find nothing that's within a factor of 1,000 or 10,000 of that concentration in that animal assay, that's pretty powerful information.

I mean, it doesn't answer all the questions. It doesn't answer dynamic, you know, possible really, you know, sensitive populations and these kinds of things, which we like to try to address in risk assessment, and whether we're doing it on an internal dose basis, or external dose basis, we're woefully unskilled at that at this point, but it provides you with very powerful information.

And we have quite a number of chemicals for which the chronic bioassays included tissue and/or blood concentration measurements during the assays or in parallel experiments. And that really provides very nice information. It doesn't require a pharmacokinetic extrapolation or model. It really just requires kind of -- you know, they were here and, you know, we're going to set a benchmark, you know, down here. So that's one approach.

The urinary biomarkers almost always are done on a mass balance basis. We know -- we have human volunteer studies in many cases where we know you put this much of the chemical in, you get this fraction of it out as this

type of metabolite in the urine over the course of 2 days or whatever.

But that fraction is just a simple mass balance if you're restricting yourself to thinking about chronic exposure conditions, which is sort of the context of the reference values

And so that's a pretty simplistic way to do things. It doesn't tell you anything about internal doses, but it says if EPA has said that one microgram per kilogram per day is a tolerable chronic dose, we can predict the chronic urinary concentration that's going to be associated with that intake. So that's another approach.

In some cases, we have very highly developed PBPK models. Toluene is an example. The risk assessment is based on human data. We have a lovely pharmacokinetic model. We can account for SIP 2E1 variation, ontogeny of SIP 2E1 from neonate through childhood and to adulthood. We can do all of those things in the PBPK modeling with relatively robust results.

And, you know, that's a whole other kind of thing. That's the exception not the rule. But, you know, so there are a variety of approaches, and it's dictated by the data that are available. But also just in terms of kind of when you're thinking about a steady state chronic

scenario, a lot of things become much simpler than they are when you're thinking about things, which you may actually really be interested in, which are these kinds of developmental things. But that's not typically how we do our risk assessments either.

So it's -- you know, again the BEs kind of carry with them the limitations of the risk assessments that they are derived from. So short answer, long answer.

DR. ZEISE: Okay. Anymore questions?

Okay. Well, we'll take a break and come back at 3:30 by this clock, and we'll have a panel discussion.

(Thereupon a recess was taken.)

MS. HOOVER: Okay. We're going to get started with our afternoon discussion. So if the speakers could come to the front of the room.

We're going to get some of the details worked out there. I just wanted to first for anybody listening to the webinar, they should again feel free to Email biomonitoring@oehha.ca.gov. And also it would help Amy who's going around with the microphone if you raise your hand when you have a question, so she can see it from the back as well.

And what we did just now was we had a bunch of questions. Obviously, this is an interesting topic and we have lots and lots of questions, but we don't have a lot

of time. So we have about an hour and a half total for this part of the program. So what we did was we narrowed down the questions and focused in based on some of the discussion today on some of the key questions that we'd like to hear from you on.

And we want to hear from both the speakers and the audience. So we're going to try to be doing some strong facilitation to try to keep people to really speak to the point and be succinct, in terms of giving your opinions on these different questions.

And some of these questions are designed to try to be broad enough to capture all the varying perspectives. So feel free to offer your perspective like you're asking the wrong question, you know, that kind of thing too.

So we're going to just start with this question, just this general question about what types of approaches -- actually, first, I'm going to run through the 3 questions so you see where we're going with it and then you can get an idea of how it's structured.

So the first question we've changed it just a little. We want this to be a general discussion of what you think we should do to understand and interpret biomonitoring results for the individuals and at the population level.

But then we ask a more specific question around this same issue that other than measured levels in relevant populations, should we use comparison levels in blood or urine to provide context for biomonitoring results? And if so, what types should we consider and for what purpose would they be applied. So that's just sort of a more specific question from the general question.

And then we do -- still would like to talk more about multiple chemicals. So this question is just a little reframed. And that is how should biomonitoring results be interpreted, given that there are multiple chemicals, including chemicals not being biomonitored, that act in the same way or produce the same health effect for individuals and for sensitive populations? So we're bringing in the sensitive populations there.

So let's get started. And I just want to hear some panel -- after hearing today and hearing the audience questions and what the Program is trying to do, if you could just offer, you know, some brief opinions on what approaches you think the program should be using to understand and interpret biomonitoring results? And you can speak to either individuals or the population level.

So, Panel Members, go for it.

Dale.

DR. HATTIS: Well, I guess, I would try to make

some kind of integrative synthesis of -- you know, that's in terms of risk or impact for some specific kinds of -- like, for example, if I have a series of relationships between birth weight and exposures to different chemicals or if I have a series of potencies, I want to interpret the biomonitoring results, you know, back calculated into exposures, if I can, maybe even steady state exposures, and say, okay, what is the relative significance in terms of population level, gram changes in birth weight, that's indicated by my biomonitoring data?

Because at the very least that could give me some priority setting information for exposures that could warrant greater versus lesser public health attention. I did that recently for a series of standard air pollutants, where basically I could quantify -- I had some, you know, published study that quantified interquartile ranges of the air pollutants. And interquartile ranges that were indicated of the birth weight effects, so I could easily integrate those and say, okay, what was the population level changes of particulate -- the PM2.5s versus the nitrogen oxides versus the other. It turns out that the PM2.5s were a little more population impactful than a couple of the others, but the others were all close.

Well, I think that gives me some preliminary priority setting information for the standard criteria air

pollutants. So I think if extended to a larger extent of exposures, that would give you some information that could be program informative.

MS. HOOVER: Other speakers want to comment on this general question? For example maybe, Amy, say something.

DR. KYLE: Did you say me?

(Laughter.)

MS. HOOVER: I did.

DR. KYLE: I thought I'd talked enough already maybe. But I mean, you know, I can't answer a question like that unless I say -- unless I know, well, what are you trying to accomplish with this program? Which maybe isn't entirely clear, you know, or is it?

Like, what are we really trying to accomplish here to improve public health? And what audiences does that give you in terms of who needs to understand the data and what do they need to understand about it? Those are the kinds of things you think about when you're trying to translate scientific information for other audiences is what does this mean in this other world or context and how can you give it the right significance for that?

So it really depends. I mean, are we trying to engage with our larger environmental health system here? I mean, are we trying to identify things that are really

not being managed or -- you know, what are our larger goals for this? I think it just bears a little bit more discussion.

And for individuals, you know, I think I've already discussed that. So I don't know that I need to comment about that again.

MS. HOOVER: Other speakers. Comments on this general question.

DR. BAHADORI: Do you think you might answer some of the questions that Amy raised and maybe that will help.

MS. HOOVER: Well, I mean, I laid out the talk that Amy missed in the morning about, you know, like the context for how we're viewing it. So basically, you know, this is obviously a growing program. And we have these various goals that are stated in the legislation on various mandates.

And one is that we are to return individual results. And it doesn't say in that actual part of the legislation you have to provide advice on follow-up steps. And it has very specific language about if the chemical and physiological data indicate a significant known health risk. So that's actually in the legislation. So that's -- we're supposed to figure that out where we think we can. So that's one side of things is the individual side of things.

But there is this larger issue about evaluating the efficacy of public health efforts to reduce exposures to environmental contaminants. And that's what George has been alluding to as well. But that's part of the purpose of this program is to help the State look at -- you know, look at how effective certain programs are being.

So that's kind of the way that we framed this. But, you know, I obviously heard all that you were saying and about that there's broader issues involved as well. I don't know if Rupa or George or Lauren want to say more about that, or panel members or SGP Panel Members as well.

DR. DAS: Well, Rupa Das, California Department of Public Health and Biomonitoring California. I guess in terms of, Amy, your question about what is our goal? I'm not sure I'm going to be answering exactly what you're asking.

The way I see the goals of the Program, the way we've thought about it as a Program is to fulfill the mandates. And the mandates being, you know, in terms of letter of the law to return results to individuals. And by that we mean not just the actual numeric results, but to return it a meaningful way, which is to interpret to the best of our abilities in terms of what does that mean. And that will depend chemical by chemical as to how we can interpret it.

And then to use those results to say something in a public health context. So in addition to returning results to individuals, we would also -- we're also tasked with interpreting what it means in a public health context in terms of how effective are our -- I can't remember the exact goal, but how effective are our public health efforts. How can we use biomonitoring results to say something about our public health efforts.

DR. KYLE: Well, just to say a short word about this. I know you have something to say. You know, the thing about returning results in the development of the legislation, and maybe Davis would want to comment on this or Sharyle, but, you know, that was a right to know provision of the bill. That if you're going to have this program, people have a right to know their results.

It wasn't exactly the purpose of it though to return results to people. It was more like something that needs to be done along the way, needs to be done well. And it raises issues, and I recognize that.

And you're dealing with them. But it seems like maybe -- you know, and I will also say this program is growing incrementally and you all have been very resourceful in finding resources and ways to put together stuff. But maybe it's -- it might be time to really think -- have a little strategic thinking about well, what

are the questions you can answer with the kind of results you're going to have, and how do they relate to the responsibilities of CalEPA and the Department of Health.

And, you know, what are the things that you could shed light on when we think about it from sort of a public policy kind of point of view.

Honestly, I don't know enough about the details of everything that you're collecting to be able to say what I would do. But I could investigate that and give you a different answer. But it just seems like maybe that's the next thing to think through in the evolution of the program.

MS. HOOVER: Yeah, I realized I should say, you know, stepping back from some of the interpretation issues, just like what the legislation was setup for, which is to figure out what levels of chemicals are in people and what the trends are over time in a representative sample of Californians. And we're not able to do that right now.

So that's part -- you know, the legislation was framed around that as a major goal of the Program. But like you say, we've had to, you know, do something a little bit different than what the legislation laid out, because of resource issues.

I don't know. George or Lauren, did you want to

add anything to that.

Oh, I'm sorry. Dana, go ahead.

DR. BARR: I just want to add something that, you know, maybe one kind of rudimentary thing you could do is -- somebody brought it up in their presentation today was some sort of reverse dosimetry to try and figure out how -- if a chemical measured in our body was a maximum dose, how that would relate to a reference value that you might have in the state. And if it's 100 times below or 200 times below or 1,000 times below, it gives you some indication that you're doing something right to protect the health below the -- the health of the individuals below these standards.

Now, one question I have, and I don't know, when you report the results back and you say, okay, we don't know any health risks that are associated with this or whatever you might say, what happens if 10 years down the line we find out that there are risks associated with those low levels, and are there any kind of legal repercussions or -- it was just something I was curious about.

MS. HOOVER: Yeah. That's actually -- actually, Amy and I were talking about this in the break about that issue that she pointed out with lead that we've seen with mercury. You know, the more you study, the more you find

out. And we already kind of know that, that whatever we say now we might not agree with ourselves later.

And the question is, what's -- I mean, to me I feel like we still need to say what we do and don't know right now. You know, I feel kind of an obligation to say what I do and don't know and along with the uncertainty. But, Rupa, do you have another angle?

DR. DAS: Well, just in response to your question, Dana. I think we part of -- someone raised the issue of the informed consent process. And what we tell participants is it's really important to tell them what we're going to tell them, what we can't tell them, and what it might mean for, you know, our legal implications in the future. So our informed consent process currently says that we will tell them what we know and we may not be able to tell them the health implications of the findings, but we'll tell them what we do know. So I think in terms of disclosing information now and how it changes in the future and what it means in terms of our legal obligations, I'm not an attorney, and I can't interpret that.

But I think we leave open the possibility that the information will change. And we've had discussions actually in -- when we get approval from our IRBs about what will we tell participants if the information does

change. If we find -- for example, if we do new analyses and those -- the health implications of those are different than what we are able to do now, do we need to go back and give the participants that information?

I think it's a constantly changing field and our information -- our informed consent process leaves open the possibility of going back and giving new information to participants if we find new things in the future.

So I don't think what we tell them today is necessarily binding and has legal implications. If we have new information, we can go back and change it.

DR. BARR: Well, I think then perhaps one approach could be to use this reverse dosimetry. One thing that concerns me about doing this and one thing I think I kept hearing a lot from people is well biomonitoring tells us what people have been exposed to, or what's in people's body. And that's true about the chemical we're measuring, not necessarily about the parent chemical.

And so I think it's important to remember that it's about the -- if we're measuring a metabolite in the body, all we can say is that metabolite is in the body. We don't know if it necessarily came from the parent chemical.

So if you do a reveres dosimetry approach, you

kind of have to assume that everything came from that parent chemical. And then what happens if then you have a range of exposures that then exceed that reference dose, you don't necessarily know if it's because they really did or because your biomonitoring was overestimating your exposure to that chemical.

So I guess in a worst case scenario, if you did that reverse dosimetry and everything came back orders of magnitude lower, then you can at least give them some hope that your exposures are lower than what the reference standards are for the State or for the U.S. or whatever.

So that might be one rudimentary approach, but I think Tina might have a more sophisticated approach.

DR. BAHADORI: No. I do, but I'm not going to share it, because it's too sophisticated.

(Laughter.)

DR. BAHADORI: Anyway. I actually had 2 questions. One is whether your IRB, in addition to allowing you to go back and supply additional information, does it actually allow you to do additional analyses as the science evolves?

And then I have a follow-up question to that.

DR. DAS: So your question is, does the IRB allow us to do additional analyses? So as part of our consent process and as part of the sample collection, we are

asking participants if they would consent to collecting additional samples for archiving, which would allow us to do additional analyses in the future.

And if they consent to that process, then we do archive the samples, and with the understanding that we would do additional analyses in the future.

The question of how those additional analyses would be returned, that we'll have to deal with in the future.

DR. BAHADORI: Hasn't been addressed.

DR. DAS: Because some of those might be deidentified, so if they were deidentified, then we would not be able to return them.

DR. BAHADORI: So to that point alone, I'd say it's then particularly important, if you're going to have conversation with some of the colleagues in California who are evolving and developing new methods to develop and interpret biomarker data beyond what is being done right now, to have that conversation, because it may impact how you collect, how you store the samples. So that's sort of an aside.

But going back to this question, I'm wondering if a safer thing to do, to me even a more ethical thing to do, and maybe somebody like Sharyle can correct me, is that you provide the numerical data as to the letter of

the law and what the expectation was from a right to know perspective, that you provide that to the individuals. But instead of an individual interpretation of the health relevance of that data, that separately a report or an analysis be done to contextualize the overall data. Because I will submit to you that there's -- for a majority of the chemicals even using reverse dosimetry, there's very little you will be able to say.

So it might be better to have some kind of a more sort of all-encompassing analysis of the biomonitoring data, that says maybe contextualizes the data, maybe analyzes some of the chemicals, that you have some ability to analyze for and tells an overarching story that says, that unfortunately we don't know yet what else to do, but we will let you know if we find out. But sort of a more of a general picture, than an individual -- because when you -- as a mother, if you gave me individual information about me or my children, I would feel obligated to think of something to do.

And if you can't tell me what to do and no one else can tell me what to do, then the whole process becomes very demoralizing and frustrating. And, you know, it becomes a barrier, in my opinion. But if it's part of a sort of a general context, then, you know, it's like everything else, whether I use a glass bottle or a BPA

ridden bottle, at least I have a personal decision to make that is part of a bigger context than me.

DR. AYLWARD: Can I make a comment, Sara?

MS. HOOVER: Yeah, sure. Go ahead.

DR. AYLWARD: You know, I think that the limitations and the concerns about communicating about risk assessment-based values, whether we use BEs or whether we use -- do a reverse dosimetry on an individual basis and compare back to reference doses and those sorts of things, I think that those concerns are really well founded. I think that the risk assessment-based values are very hard to interpret, even for risk assessors in terms of what individual risks or population risks might be, because of the way we've done risk assessment.

And although I think we're moving towards a more informed and intelligent way to do risk assessment, you know, we haven't done it for anything yet. And so if we're talking about measuring tens or dozens of chemicals and trying to think we're going to have something from that that we're going to be able to say to people, I think we'd be -- is not going to make sense.

And so I'm -- although, you know, I've worked very hard to provide these translations, I recognize that they're really principally a risk assessment tool. They might be useful for a physician somewhere, somehow if

they're really well informed in talking to people. But they're really not going to be very meaningful, I think, for individuals and particularly when we think about cumulative risk considerations and things like that.

What I would suggest, in my own personal, if I'm sitting in the hot seat and needing to think about communication materials for individuals, I think I would have the following elements:

I would have both the range of values observed in your own program, in your own -- in your population that you're looking at. I would have the you know, 5th to 95th percentiles from the NHANES program. And perhaps those 2 things will look very similar, and perhaps they'll look different and will be interesting to people along with where that person's values fall.

For a very select number of compounds, I will have information, for instance, with lead that, you know, as we think about lead, lead is important for childhood development in particular. And I would -- as an internal group, as hard as it is, I would set some level, whether you decide to go with the old value or a more conservative value, set a level and say anyone whose values are above this, we're going to go back and talk to them and think about, you know, what that means. Lead and maybe cadmium and maybe mercury are, you know, chemicals, perhaps

arsenic, where we have --

DR. BAHADORI: Triclosan.

DR. AYLWARD: -- human data. Triclosan. We have human data for triclosan.

(Laughter.)

DR. BAHADORI: We will soon.

DR. AYLWARD: Okay. You know select those chemicals where we have this really a foundation of information that even if we don't perfectly agree on cutoffs or cut levels, we can be informed about what we tell people about those, and have messages associated with those. I agree with Tina that having an overall discussion in terms of what the overall results of the program are going to be used for, what they -- what we think they mean in the context of other surveys that have been done.

And then I agree, Dr. Culver had brought up the issue yesterday, I think, about your going to have people who are outside the NHANES 95th percentile. And I think that Ruthann's, you know, discussion about who's high and why, you know, even if we don't know that there's a health effect associated with being above the 95th percentile for some chemical, it's probably worth thinking about going back to those people and being able to do follow up with them to understand if there's something that can be

learned from that and advice given to them.

And finally -- I'm sorry I'm going on long -- but to the extent possible, you know, whether people are high or not, when you give them biomonitoring data, some people are interested in learning how to reduce their exposures.

So even in the absence of a health context, they're going to be interested in saying, geez, you know, do I really need to use that product or whatever. But I will say that it's very important that that information about exposure sources be accurate.

I keep seeing that, you know, when people are exposed to trichloroethylene in typewriter correction fluid. And you know, I don't know whether people are still exposed to trichloroethylene in typewriter correction fluid. That's data from 20 years ago. And I don't even know if it's still being used.

And so, you know -- and I was describing to Melanie Marty earlier that the FDA has been analyzing personal care products for phthalates. And putting aside DEP, which is used as a carrier for a variety of fragrances and is quite prevalent, they don't find hardly any phthalates in personal care products anymore. They've done hundreds of analyses over the last 4 or 5 years. They've been taken out of most personal care products.

So if you go and tell people that their personal

care products contain phthalates, and so they're going to stop using shampoo and start washing their hair with bars of ivory soap or something, you know, you haven't done them any favors. They don't know what they're doing and they're not actually interdicting the exposure they think they're interdicting. And so that information really does have to be accurate. And I would suggest that with your analytical capabilities, your labs, you know, might start thinking about studies that might, you know, go out do some market basket studies and think about some of these things. So anyway, I've gone on too long.

DR. BARR: Can I just follow up on that. Sorry, Lesa.

But when you're reducing your exposures to many chemical, you're replacing them with exposures to other chemicals that you're not necessarily measuring. So, yes, you can probably reduce your BPA exposure by using BPA-free containers, but now you have exposure to something else that might be in there. And, of course, if the last EHP article is to be believed, you may have more estrogenic activity from that exposure as well.

And so I think that we need to also put that in context, that we're only measuring a handful of things. And you probably -- I don't know if you'd scare somebody by saying you have lots of chemicals in your body, but if

you say everybody has lots of chemicals in our body. In fact, our body is one big walking chemical, because that's we're made of.

It may help allay some fears. It's kind of interesting in my survey of Environmental Health Class, we actually do a risk perception. And I'm no risk person at all, but I do teach it on TV.

(Laughter.)

DR. BARR: Or at least at Emory. But we had this one exercise where you had to rate the relative risks associated with certain activities. You know, one would be skydiving, one would be space travel, one would be consuming illicit drugs or whatever. And it was really interesting. We kind of compared it to a 1997 paper that was published in Science.

But basically the things that people were most afraid of were -- or thought that biggest risks were associated with were the things that they didn't know anything about or that the things that they felt like that only isolated people would be doing, like space travel.

But things that everybody did, like bike riding in heavy traffic or mountain climbing, they didn't see the same risks associated with that. So I think maybe if they realized that they're more like the average Joe too and they don't stand out, then that would help to allay some

concerns about their potential risks.

MS. HOOVER: I think Asa has been waiting to make a comment. So, Asa, did you want to jump in here?

DR. BRADMAN: Actually, I found this discussion really interesting. And I think actually the discussion is coming to, in some ways, a consensus, at least that I agree with. And I just want to be clear earlier I made some comments, and I wouldn't want to make -- there be a misperception. I think, I'm very concerned about the reporting back requirements of the legislation in California, and if and how we would report a health interpretation to individuals.

I think it's imperative -- there's a responsibility for the programs to evaluate the public health implications and the population implications. And I'm afraid that if we report individual risk interpretations, that that could become a fraught process, and it could, you know, delay progress of the program. And I think the ideas that have been laid out here have perhaps -- you know, if there are a select few where there's good information, or maybe limiting it even to something where there's an FDA recognizing diagnostic test and interpretation, that where there's some certainty, we provide some information. And where there's not, as part of the consent process, use that consent process as a

conversation, so people know what to expect.

I think that's really important. And I know -- I mean, I feel like people who participate in this, there's kind of a civic duty in a way. I'll out myself. I'm in the Kaiser RPGH EHS study. I gave them a saliva sample. I don't really expect to get results back. If I did, you know, I can only take it one way or another. But by participating in the study, I'm hopefully contributing something. I think people take that attitude.

Certainly, in my interaction with participants in studies that I've been involved in, people don't expect an individual gain by being in this study, but they do expect to contribute something to a larger effort.

And I think what's important with the study though is to make sure you don't take from the participants. And I think this new philosophy of reporting results back, you know, sending letters to participants, not just parachuting in, taking a sample, and leaving. This new philosophy, I think that's governing a lot of environmental health research, because of the environmental justice movement, has really moved forward the whole process of interaction with participants.

But we shouldn't -- we shouldn't -- again, we shouldn't get bogged down in trying to answer questions

that we can't answer. And I think participants can know that and understand that through the consent process.

MS. HOOVER: I wanted to give Ruthann a chance to pipe in here, because you didn't speak to this question originally. And, you know, you've been involved in these studies and interacting with participants. So do you have some comments on what's been said so far?

MS. RUDEL: Well, I'm thinking about what Asa just said. And I was always conflicted about putting in the risk-based screening levels into those graphs. Although, we ultimately decided to do it, because it is information that -- so that I -- I was interested in, and so I can just -- I think it's logical to assume and reasonable to assume that the participant might be interested in it as well. And that, you know -- but there -- as I tried to kind of show when I went through that report-back graph, say, with looking at the levels for the health-based guideline values for the different phthalates, you know, there are a lot of problems in the underlying data, and then there's a lot of missing data.

But maybe that needs to be just communicated as a part -- you know, as a part of the program. I'm not sure that the solution to that is not -- is withholding the data, but I don't know. And, I mean, I really don't know where I come down on this. But I do kind of have a

reaction to withholding information that I myself would look for. If I was in the study, I would look for that information. I would want to see it, what's a health-based -- any kind of guideline values. So I can just assume that somebody else in the study would want that also.

I'm thinking about the level of effort involved in coming up with information that is useful to people. We talked about all different components of what people might want to know, like, you know how to avoid it, and the health-based value. And so that might actually -- thinking about that is making me think about being more targeted in the analyte list to chemicals where you actually do have a policy -- a reason to care about right now, and that you're willing to invest the effort in looking at the risk assessment, maybe even doing some additional testing, like putting it throughout the EDSP, Endocrine Disruptor Screening Program, protocol, or putting it through the high throughput screening.

So that there's -- and I guess Lesa suggested actually, you know, testing products and things to see what they're in. And that's also good. And maybe if industry could be encouraged to provide some of that information, that would make it a lot cheaper for the State.

The fact that EPA had to actually go buy samples of dental floss from the pharmacy in order to test them for perfluorinated compounds is just -- you know, it's kind of -- it's -- I don't know. It bothered me.

(Laughter.)

MS. RUDEL: And, yeah, so and then -- so those are my -- that's my thinking. I'm thinking about in terms of -- you know, that to think more -- I guess be selective about the chemicals your going to look for.

But then I think the way -- because this is not turning out to be a representative population-based Biomonitoring Program. It's being done in the context of some specific, some special studies. So the target analyte list is going to be informed by really, you know, what those studies are and what they're trying to find out. And I wouldn't want them to be restricted by -- necessarily by, you know, those other considerations. So that's kind of countervening.

And then I just feel -- I feel, you know, pretty strongly that in representing comparison exposure levels and exposure levels from the study, although it's important to put the median, the range, maybe the 5th and the 95th percentile. The maximum, even though statisticians hate it, provides really important information and should always be included.

MS. HOOVER: I think there's a question back here. If you could identify yourself.

MS. RYAN: Okay. Susan Ryan

MS. HOOVER: You need to hold it up to your mouth and speak directly into the mic.

MS. RYAN: Susan Ryan.

MS. HOOVER: Closer. Right into it for that one.

MS. RYAN: Susan Ryan. I'm just here as an interested citizen. It seems like you guys are really heading towards some exciting stuff. I'm really happy that you're doing what you're doing. And it seems like some of the questions that came up about having to respond back to people who actually participated should be like your spring board for what you do next.

And I didn't hear the beginning of the presentations this morning. I tuned in at like 11. So I don't know if you already have plans to expand your studies to certain populations, like maybe kids who are dyslexic or, you know, just pick groups that are of major concern to a lot of people, especially things like -- we've noticed increased allergies in the children and just pick out things that are interesting and then recruit volunteers for that group as well.

And you can use the idea of what's happened here. You know, you feel a responsibility to be able to respond

to the people that participated in the study and you can't spend a lot of money. Your resources are limited. I don't know what your other limitations are, but you might be able to work with other organizations like the American Lung Association or the American Cancer Association and get some funding from them for some of these.

MS. HOOVER: Yeah, we had actually had a discussion like this yesterday. So I can -- yeah, I can send you some information, but that's still -- you know, thank for your comments, yeah.

And I think, did you have a question too, Sharyle?

MS. PATTON: I'm Sharyle Patton from the Commonweal Biomonitoring Resource Center. And just a couple of comments.

Of course, we do fairly targeted biomonitoring. We go into a community that has some real concerns. But we're finding that any kind of general audience, people are really hurting. I mean, there's probably not a family that doesn't have a close family member with some kind of cancer or some kind of developmental disability. So they're looking around for answers for why.

And so doing biomonitoring research with a community is not going to give answers to that kind of question, but it opens up the conversation, and that's

what you're really doing. I think we're doing when we do biomonitoring, we're starting to help communities ask questions and we're starting to develop or create a space for community processes to happen.

It's always been very powerful in communities for them to talk about, among the participants, what their results were and where their reactions were. And unless they can kind of share that kind of information in a very deep way, it's much easier to talk about all the uncertainties and all the things we don't know.

But nevertheless, get a sense that pay attention now to what's going on with toxic chemical policy and what you can do at home. And keep paying attention to the statistics in the same way as you pay attention to the statistics of the -- what's reported on the news every night, the intersection with the car crash that happens. Not all cars crash there, but some do in someway, and some don't. And so try to figure that out. Some people seem to respond differently to toxic chemical pollution. Others do not. Why? What do we know about that?

So it's an ongoing conversation. And it's a relationship as well between a researcher and the community and the individual. We talk about in California the slow food movement, all right. Well, this is the slow research movement.

(Laughter.)

MS. PATTON: We're really taking this on and it's going to be a conversation we're going to have forever.

MS. RUDEL: Know your scientist.

(Laughter.)

MS. PATTON: We all know biomonitoring is a lot slower than we want it to be, and it does take forever. But in that period of time, you are building a relationship with a community and helping a community develop the processes to make good decisions, as whether it's going to be done on an individual basis or a community basis or whether it's going to be in the personal realm or the political realm, you start those processes. I really think that's what it's all about. And I think that's really what we need is communities can then take on these questions and think about them.

Toxic chemicals and the fact that we all carry these chemicals in our body is evidence of kind of a failure of many of our prevention policies. Well, that's one crisis we're facing, but it's also the climate chaos changes are happening as well. We need communities that can really think.

And like Politics, I think biomonitoring, all biomonitoring, is local. Every piece of data is really a personal story. And that's -- I think we need to talk

about that and realize that more.

So I just wanted to make those comments.

DR. BAHADORI: Sharyle, are you advocating then that the data just be given to them or are you suggesting that conversation contextualize it as well?

MS. PATTON: Well, every piece of data goes into a personal story, into a home. And so when we give -- we do give data to people. And, of course, everybody looks at the data and they want to look at who's low and who's high as if it's some kind of contest. That's the first thing they do, they compared their levels to somebody else's in the community or from some other study.

But then that opens the conversation about what high levels mean, what low levels mean, what we know and what we don't know. And it's a conversation that goes on for quite some time. I'm not sure it ever really ends with the people we've actually tested. But, yes, we think you talk about personal levels to the individual, but you take on certain responsibilities to tell all we know and all we don't know about how toxicity is moderated by so many factors, and where can you work.

And, of course, some communities will look at this information and say we really want to be active about this in a very particular way. And other communities will say, this is interesting, but really what we're dealing

with is more important is drug dealers moving across the California Mexico border or we can't keep our kids in high school. And so each community is going to respond differently.

But nevertheless, they will have processes in that community now to make some decisions. And they will have the idea that they at least should be paying attention to how these toxic chemicals can cause harm. There's a possibility. The fact that there are hundreds of untested chemicals in their bodies that nobody knows anything about. So this also becomes part of their framing about how they make decisions politically and personally.

I just think that's so important. It's one of the tools that we use. I was talking to a colleague earlier -- I'm talking too long. Just to say this last point, that when we are organizing around the Stockholm convention, which is the convention that gets rid of POPs chemicals, we were working with groups, community groups in many countries. And many of those groups joined us or the network, because what they wanted to really talk about was, for example, land redistribution or wealth redistribution. And you can't talk about that in many countries without getting shot. But you can talk about children's health and toxic chemicals, and that's the way

to organize a community to start being engaged politically.

And I think not that that's true in this country, but to a sense -- in a sense we are talking about toxic chemicals and regulations as a surrogate for other kinds of conversations that haven't quite emerged in this country. So that's also something to think about.

MS. HOOVER: Did you have --

MS. RUDEL: I just have -- thanks, Sharyle, for that insight. And I had -- I'm excited to be part of the slow science movement --

(Laughter.)

MS. RUDEL: -- even though, it does seem awfully slow sometimes.

(Laughter.)

MS. RUDEL: And I had an afterthought about the last comment I made about being more focused with the set of chemicals, so that you're willing to invest in characterizing exposure sources and health effects. That maybe an opportunity for doing more exploratory wide-ranging, like let's look for lots of different chemicals, and just -- and see what we find. Is there an opportunity to do that on deidentified, like blood bank or other kinds of samples, where you're not going to be facing a report-back situation.

And then -- so there could be different -- you know, there could be different ways that you -- that you explore different kinds of questions, and that this issue of reporting back can be one of the things that's considered in deciding how to go forward.

MS. HOOVER: Dale, did you have a follow-up comment that you wanted to say as well? I thought you were leaning in.

DR. HATTIS: We've talked a fair amount about reporting back on an individual level relative to other individuals. And I think that there's some chance that some of the time you want different levels of aggregation in the analysis, that, you know, maybe is your community different than other communities in its distribution of some biomonitored chemical?

Or is -- you know, are there some kinds of biomonitored things that are different as a function of fish consumption or different as a function of age or gender. There's a lot potentially in this kind of data that could be of interest, you know, in shaping our picture of overall exposures. And it's -- and that is just -- we need to leave open, to some extent, the question of not only individual versus group average or group distributions -- and I like the distributional representation that you guys did -- but different subset

analyses that creativity may suggest itself.

MS. HOOVER: Okay. Let's see. I think I'm going to -- before we go on with this, I want to just also do one thing, because we're losing time. I think we've actually already addressed this question, but I just wanted to flash this up, because we've been talking around this, about should we use comparison levels in blood or urine to provide context for biomonitoring results? And if so what types and for what purpose?

So I think we actually already discussed this and we got a lot of input on looking at things that we already know. And I wanted to fill you in that actually DPH already has a protocol for lead, so that's been worked out. And we're working on one for mercury. And so we are kind of doing the logical thing of tackling things that we would feel most confident about.

But I just wanted to see if anyone had, you know, kind of any other comments on this particular issue about -- because I feel like what Ruthann said is very true, which is I also will say I've been biomonitored and I asked for my results, and I want to see them. And I know that I may or may not understand those results. But I also would have that reaction of I'm going to go look. You know, I'm going to go look at everything that I can find.

And we've had this conversation back and forth about -- part of it is I'm an informed consumer. You know, we're informed consumers. We understand the uncertainties and what it does and does not mean. So if we know there's a value out there and it has some meaning, do we have any responsibility in sharing that? And if so, how?

So any other comments on this particular question about comparison levels from anyone.

George.

OEHHA ACTING DIRECTOR ALEXEEFF: George Alexeeff with OEHHA.

So I just actually -- I'm going to -- I will answer your question here. But I was going to go back to what Amy was saying earlier.

So it takes me that long to digest what you say, Amy. Anyway, so I was thinking about, you know, the question well what's the purpose of the Program. And, you know, just in terms of my understanding of the purpose of the program, there was a strong initiative by population, subpopulations to understand what they perceived as their increased risks from chemicals. And they desire to have this type of information available.

So that was part of it. And part of the whole discussions of this bill became apparent to us that in

order for us to really actually ultimately give information to populations, we had to have some information about the baseline. And in order to have -- and so the question was, well, what about the NHANES baseline?

So that raised the other question of, well, we have a lot of populations in California or the demographics in California are different than the U.S., so the question is, is California's exposures different from those in the U.S.?

So these are the kinds of questions that were coming out. So one was, are there exposures in certain subpopulations within California which are greater than the kinds of exposures that are generally seen in NHANES? And particularly we were concerned was about the Asian community, which is very high population percentage here, but not nationwide necessarily.

And then there was the concern that I think that Dale was mentioning in the sense that were there particular diseases that were associated with chemical exposures? And so that was another ultimate goal to try to see, could one determine that, which would require, of course, other sort of analyses.

And then the other question was trends. There was the issue of, well, there's an increase in this

chemical, and -- you know, like PBDEs and such were increasing in various populations. So could this be helpful for California to understand trends, increasing certain chemicals?

So, I mean, those were some of the purposes that were raised. And then also the one I had mentioned yesterday about the idea that, well, assuming there were chemicals increasing in trends or assuming there were populations that seemed to be excessively exposed, what can risk managers do about reducing those exposures? So I think one would want to look at relevant populations and compare them, both within, you know, communities that might be greatly -- more greatly exposed and subpopulations within the state as a whole that might have a different exposure sort of scenario then than others.

MS. HOOVER: I think Gina walked up to take the mic from you, so I think she wants to say something.

(Laughter.)

DR. SOLOMON: I just wanted to add one more point to the list that George mentioned, because I think it's relevant to this question, which is one of the things that has distinguished the California Biomonitoring Program has been the interest in looking at emerging chemicals that might be of concern in the future, things that are newly coming onto the market to replace ones that were known to

be of concern, et cetera.

And if one tries to apply a model in which we're -- you know, I mean, it becomes way harder basically to put those into context. They're not part of NHANES. They are, you know, trying to derive any kind of Biological Equivalent number, probably not do -- almost certainly not doable for most of them, because they're so data poor.

And yet, the Scientific Guidance Panel and this Program has really identified those as a direction that we -- you know, we want to pursue. And so, you know, I wouldn't, at least, personally want to see that effort slowed down in any way, because of some need to, you know, figure out a context to communicate before we went out and started gathering that information, because by then, the whole point of being ahead of the curve would be lost.

And so I think that we do need to think about Amy's point and the, you know, what are the real priorities of the Program and how do we keep moving towards those while also fulfilling the important mandate to communicate results, you know, but not letting that get in the way.

MS. HOOVER: Oh, go ahead, Amy. And then I want to go back to some other hands that I skipped over earlier.

DR. KYLE: I'll be brief. You know, I think there's different kinds of context and maybe that is one thing to think about. That, you know, you'd expect a different kind of context for an emerging chemical than lead. You know, and maybe that's part of what needs to be communicated here is that we're on way different points of the trajectory of research on some of these different chemicals. And everyone -- everything won't have the same kind of graph and this is why, because I completely agree with you. But on the other hand, that could be communicated, what you just said.

MS. HOOVER: Ulrike.

DR. LUDERER: So I've been kind of just listening to all this stuff and these really interesting conversations that we're having here this afternoon. And one of the things that kind of has just kind of occurred to me in listening to all of this is that maybe what we're kind of moving toward is maybe a different conceptualization of what does report back mean.

I mean, we've been talking about really this idea of, you know, giving individuals their individual results. And I think that's really important. And obviously, the law, you know, mandates it, you know, and potentially giving it -- and I think I'm in favor of the idea of putting it in, if it's available, relative to data, such

as NHANES data or population-based data.

But then kind of given all the problems that we've been talking about today, all day really, regarding these risk-based reference levels, you know, that we've been talking about again this afternoon, my kind of -- what I'm sort of moving toward here is that maybe the report back regarding the potential health risks, if any of them are known, you know, really should be more -- could potentially be in the form of sort of periodic summaries perhaps that are sent to the participants of findings derived from the Biomonitoring Program.

You know, for example findings regarding heavily exposed communities or subpopulations or findings relating to health effects or disease effects, if those are, you know -- if studies are done in collaboration with others, and then reporting those back in some form to the participants, so that there's an ongoing kind of, you know, communication with the participants. But it wouldn't necessarily have to be on an individualized level, where you're, you know, interpreting each individual measurement that's made in every participant, you know, in terms of their specific health risks, which, as we've kind of all been talking about, we really can't do for the majority of things that are going to be measured.

So I just kind of wanted to throw that out and see if other people have thoughts on that.

MS. HOOVER: And I wanted -- I know someone -- you had a question at the back earlier. Did you still want to make your comment?

MS. WASHBURN: My name is Rachel Washburn. I'm a sociologist, medical sociologist. I've been studying biomonitoring. I wrote my dissertation on the politics and history of biomonitoring in the United States. And I'm working on a couple papers now.

But just a couple points. I was not going to say anything, but I can't help myself. So one meta sort of point, I think, is the sort of double-edged sword. I think Sharyle it's really important to provide individuals the opportunity to have their results and to have those conversations about environmental health risks generally. I think on the other hand though, there is a way in which it sort of furthers this sort of like neo-liberal neoliberal ethos of individual responsibility and the idea that we can shop our way to safety, which is really stratified by class and education, right, not all of us have the same ability to shop our way to safety.

And I think that's a problem. It makes it an individual problem, when really it's a much broader structural issue. Certainly, there are cases where

individuals are doing something that is posing, you know, a higher risk to them, but often that might not be the case.

And then the second point I wanted to make that's more of a specific point, that struck me actually during the presentations today, as one suggestion for reporting data to individuals. I've interviewed individuals who have been biomonitored about their experience about what it means to them.

And I think in some ways being able to provide some of the complexity, I think, is important. I think it's important to simplify, so that people can understand, but I think the issues, especially around the non-persistent pollutants, and the incredible variability. We give a number, and there's this assumption that that number stays the same from day to day, hour to hour, week to week. And that's just not the case.

So I think providing people even with the charts Lesa that you had in yours, where you can see the variability -- maybe you can't do that for the participants, but you could say this is the kind of behavior that you might find with this kind of compound, I think people could understand that.

And just one last point. I interviewed some folks women who had been monitored for methyl mercury.

And, you know, our conceptual frameworks for dealing with health information just still -- we don't have a conceptual framework for how to deal with information that's so variable. So even when I interviewed these women who got a number back, they would tell me, you know, when I asked them what was your result, they'd say I was negative or positive.

So still we have to think about what are people's health frameworks and templates? What do they bring to sort of making sense of this kind of data?

Thank you very much for the time.

MS. HOOVER: And I just want to check before we go on. Is there anyone else I missed, because I think I might have skipped Davis?

MR. BALTZ: Davis Baltz with Commonweal. When this bill -- before this Program was -- became a reality, you know, it was in the Legislature for 4 years. And it was quite a chore to convince legislators why it was important. But one of the things we kept repeating was that this is a scientific data-gathering tool, biomonitoring, that is going to provide useful data for subsequent conversations on what to do with the information.

And it stems from the fact that, as we all know, there's not enough information about chemicals in

commerce. And I think the NHANES experience clearly shows this, that these data sets are very valuable. And the conversation earlier about phthalates and, you know, the anogenital distance that that came out of mining the NHANES data set to a certain degree.

So in terms of where this Program goes now, I think it's important that the Program stay focused on generating data and publishing it. And we don't want to get bogged down, as Asa said, in conversations about how do we report results to the point that it slows the Program down.

Dana made the point this morning, it's necessary to do repeated studies so that you have trends over time, and that's what we need, so we can make informed decisions.

Now that said, the statute requires us to report back results. And we had a great presentation yesterday from Rachel Morello-Frosch and Holly Brown-Williams who showed that it is being done in a sensitive and accessible way. Ruthann's research this morning also clearly -- presentation this morning shows that people actually gain some measure of empowerment from hearing their results. They don't go into panic mode.

I made the comment yesterday, you know, people are grownups. We can handle this information, and may

actually benefit. We don't have to just play defense in reporting results. There's this concept of autonomy and justice, and hopefully some greater awareness of literacy and health and biomonitoring that will prompt people to do something else to reduce their exposures and to those in their family and their communities.

And since a lot of the reasons we're in trouble now is because chemicals have been approved for market without sufficient data, ultimately, I mean, it's my hope that, we get to a point where there's requirements for a greater demonstration of safety before things are marketed.

So in terms of what we do to help people, yes, we should tell them where they fall within reference range. But we should also tell them that if they had been measured 20 or 30 years ago, the reference range would have been much different. In fact, there might have not even been a reference range, because the chemical hadn't been synthesized yet.

One of the things maybe we should consider telling people is so a history of this chemical. When was it developed and when did it come on the market, so that people can see that their grandparent may have been the first in their lineage to actually have been exposed to this thing. So it will give people some sense of the

history of this chemical, which is probably relatively short-lived in human existence and how we're going to cope with it.

So I think that could be useful information for people. But my key point here is that let's generate more data, let's publish it, and then let's have subsequent conversations in other fora to decide what we're going to do with it.

MS. HOOVER: So Ruthann, you had a follow-up and then...

MS. RUDEL: Yeah, I was just 2 points that came to my mind, but that what we found and I think, you know, others have kind of echoed this is that the people, even though they might be unfamiliar with this and they even might be uncomfortable with it, people are very familiar with dealing with uncertainty and with decision making in the face of uncertainty. We do it all the time in many, many contexts in our lives.

And, as an example, I mean, people enroll in clinical trials. And they have to decide whether they're going to, given the fact that they don't know whether the treatment will work or whether they'll get the treatment. And that's just one example.

But people, they might be unfamiliar with these specifics, but I don't think they're so necessarily

unfamiliar with the general dimensions of uncertainty and health decisions. And they might not know how to -- you know, there might be limitations in literacy and numeracy, but there's really a pretty good capacity to understand the same things that we're taking from this. So that's one point.

And the second is that the participants really varied quite a lot in their interests in this. And certainly some of the people, including some of the highest exposed people, couldn't care less. And that's fine. The idea is of giving people the option to make choices that are consistent with their values, and that's why we're doing this.

And so one of the projects we're actually trying to -- working on right now is a digital report back, so a computer-based report back that is very flexible, so it could start with very headliney kind of presentation of the data. And then it allows people to drill down as they -- in the area of what they're interested in. And in that way, it could be presented, you know, kind of with or without health data -- health kind of guideline values, depending on what people are interested in.

And chemicals could be grouped. For example, according to where we have a lot of information and some confidence in health-based guideline or a medium

confidence and a low confidence and no data. You know, and doing it with -- the no data ones are the red flashing ones. And the high confidence ones are the green ones. You know what I mean. So we so much like to leave the no data ones kind of just dissolve and disappear off the radar.

So that's, you know, just another way of thinking about opportunities that you can design methods that are responsive to what people want -- are interested in and can handle.

MS. HOOVER: Lesa.

DR. AYLWARD: Just a couple of quick comments, both related to sort of reference range. I was interested in your comment about temporal trends essentially. And, of course, for many chemicals we don't really have much of a history in terms of biomonitoring. And so you have history in terms of use and production, but maybe not in terms of biomonitoring, but for some chemicals we do.

And actually for those chemicals that we have long history on biomonitoring, most of those are actually very good stories in terms of a public health message, because what we have are, we have lead, we have the dioxins, we have PCB compounds. And for all of those, if you were, you know, a young adult in the 1970s your levels were, in many cases, 10 to 20 times as high as they are

now, as a young adult now.

And the most highly exposed people that you see in NHANES, for example, with respect to lead or with respect to dioxins or some of these compounds are lower than the medians were, you know, in the 1970s. And so they do demonstrate the power of the data, in terms of being able to both show the effects of actions that can be taken, and in terms of helping, you know, in some sense, to contextualize.

And in a related issue, and I know that many folks are very aware of this, but depending on the compounds, and particularly for the persistent compounds, you know, the reference range that gets shown to people really needs to be very age specific.

So, for instance, if you go pull data from NHANES for the 95th percentile in the population for dioxins or for PCB compounds, that level is much too high to apply in evaluation of someone for their -- whether their exposures are unusual if they're young, if they're a young adult. You need to use age-specific bins for some of these data, because a young adult -- you know, the 99th percentile for young women in NHANES for dioxins is probably about 15 parts per trillion in serum lipid. The 95th or 99th percentile for the whole population is probably about 80 or 90 parts per trillion, okay.

So if you're using that as your benchmark to evaluate data from a young woman, you're going to sorely miss who's actually a very elevated exposure.

And so just as a comment, I think people are -- I think there are plenty of people here who are quite aware of this. But it's very important in selecting that information that goes out to provide context and also for identifying the potential need for looking -- you know, looking for potential unusual exposures that that reference range be chosen appropriately.

MS. HOOVER: So I wanted to check with people here. We have a little less than 20 minutes left. We could continue the general discussion or we could turn more to some -- and maybe focus on population and talk about multiple chemical exposures. So any thoughts? Lauren, did you want to...

DR. ZEISE: It's a pleasure to do this really.

MS. HOOVER: Group, audience, continue the discussion or talk about some completely different topic for a short period of time?

So why don't we give it a whirl and see. If we start talking about the same issues, that's fine.

So, I mean, I think we've gotten a really good sense. This has been a great discussion about perspectives on talking to individuals and what should we

do, and the importance of giving some population context.

So maybe this question is something we've thought about it. We've thought about this issue and maybe it would be good to give some time to this. So how should we interpret biomonitoring results, given the fact that there are multiple chemicals, including chemicals not being monitored, that may act in the same way or produce the same health effect? And if maybe we focus, in this case, on -- I mean, it's an important issue to highlight this chemical by chemical number thing -- you know, we have this opportunity with biomonitoring to have an integrated exposure of multiple chemicals in a certain individual, as well as the population, and still we're talking about these chemical by chemical numbers.

So we wanted to kind of grapple with this issue about, well, we already know that that's not right, you know, from a whole bunch of perspectives. And this is one of the reasons that it's not right. So any thoughts from the Panel or the audience on this topic?

DR. BAHADORI: I'm curious what's integrated about biomonitoring.

MS. HOOVER: Well, I just mean that the idea that you can see a whole suite of chemicals present in one person, you know. So you know that it's not just this one chemical you're looking at, but you're looking at -- no,

we're not measuring all the chemicals, so it's not truly integrated, but you do have a broader picture of what the chemicals are.

DR. BAHADORI: So you had an initial complexity that you can't really say much about any one chemical. And now to expand that to say -- I think still all you can say is that they're present, because I would submit to you that for the majority of these chemicals, we don't know what the health effects are, and we don't -- we've learned with bisphenol A that what we thought we understood through the toxicity testing was not -- didn't reflect it the same way in epidemiological studies, for example.

Now, even without making judgment as to which is the right answer, there's conflicting answers. So then what else would you group together put in that bucket becomes additional judgment upon judgment upon judgment. That's going to just to me not make it very difficult to communicate.

So I would say that still the better thing to do is to report the numerical values and figure out a consistent story to tell in sort of one place. And then allow people, I think Ruthann said, to be able to drill in and maybe -- you know, if they wanted to tie into additional pieces of information that can help them form judgment.

MS. HOOVER: Yeah, and I really was pointing this to more of an interpretation, you know, a scientific interpretation and not necessarily attempting to convey that to individuals. And I do think there are groups of chemicals where we already know this. I mean, like Lesa looked at THMs as a group. There's certain common things about phthalates. So we do have, you know, indications of that already.

Ruthann.

MS. RUDEL: Yeah. I would -- I think that this, you know, could be an interesting opportunity to do some cumulative assessments. I think that a limitation is that, you know, so you might be monitoring for, you know, for 50 chemicals, and you know that 5 of them are antiandrogens or 10 of them are thyroid active, but, you know, 40 of them haven't actually been evaluated to see whether they are or are not.

So I -- you know, sometimes you have to go with what you have. And that might be the case, but it would be nice to have some portion of the Program where you maybe -- whatever the universe is that you're deciding to test for, maybe those can be included and tested in like the endocrine endpoints for the ToxCast or the EDSP program, so that you say, okay, well, we tested all of these, and these are all the androgen active or these are

all the estrogen active, these are all the thyroid active, and then, you know, do something -- doing something together.

And you could then actually also create mixtures and check them in the in vitro data -- in vitro assays, as well. So that could be, I think, an interesting research program.

MS. HOOVER: Amy, you had a comment.

DR. KYLE: I never fully grasped why we have to group things by endpoint or mode of action, you know, like -- it seems to me it's relevant to know even how many out of those that were tested were found, you know, a metric like that.

I think it's because when you do risk assessment, you have to have a dose response metric, right? And so therefore, that's why you always think about well it has to have the same response in order to look at them together, is that why?

Because it seems to me it's relevant either way. You know, even if you're testing 10 things and they're all different, I still -- I still think it's relevant to know whether you have 7 or 3 of those. And so, you know, I don't -- I mean, I guess I would start with the simple-minded metric that looks at kind of the distribution of what you tested for, what number were

reported in different -- in your study.

I get that there's -- that you don't -- that you're on a different track, but I'm not completely sure why. So maybe I'm missing something here.

MS. HOOVER: Well, Lauren, I mean, you had wanted to talk about multiple chemicals, so maybe you could give a little more.

DR. ZEISE: Well, I think the issue here is that -- there's a few issues.

One is that now we know as we're doing these more mixture kinds of tests that for the same endpoint, even if it isn't the same mode of action, there are many examples now where you test below threshold levels for individual chemicals. You put them together and you get -- you Get effects.

And so in thinking about the wide range Of chemicals that aren't biomonitored, as well as those that are, I think it raises issues about how we think of the margins of exposure in some of these comparisons. And so, you know, I think, Dana, you had mentioned that, well, if it's a couple orders of magnitude, you know, it's probably really good, and you might -- that might give you some confidence that you're safe.

And I think that this issue just kind of opens up that question whether or not we can actually make those

kinds of statements. So I don't, Lesa, what's your thoughts.

DR. AYLWARD: Well, a couple thoughts. You know, the idea of simply saying, well, I found 7 out of 10, all of that is, of course, entirely driven by your analytical detection limits, which vary widely across different groups of chemicals and things. So Dana worked really hard on certain pesticide metabolite analytical chemistry. But you know the folks over in the lab who were doing some of the other groups of chemicals, they didn't work as hard, so their detection limit is 50 times higher or 50 -- maybe they worked a lot harder, and they're 50 times lower, you know. Or this program has a big -- has a very large sample volume available to them and so they can get really outstanding detection limits, but the other program gets 10 microliters after everybody else gets their share of the serum, and so they have very poor detection limits.

So the idea of something being present or not present, and particularly when you're talking about across chemicals and across chemical classes, where the intrinsic activity of these compounds really varies enormously, you know, on a biological basis, I mean, we know that, even if we can't say a whole lot about the actual consequence to an individual.

You know, it doesn't really provide any

information. It's either falsely reassuring or falsely worrying. We can get down to -- I love listening to Don Patterson talk about, you know, where they're heading with dioxin detection limits. They're heading down into the yachtimols. You know, it's like really. I don't know even know what a yachtimol is. Is it furry. Does it have big horns?

(Laughter.)

DR. BARR: He defined it. You walk by the instrument and you still get a 3 to 1 signal to noise ratio without injecting anything.

DR. AYLWARD: Right. Exactly. So, you know, the whole idea of detection is somehow a signal of interest, you know, is very much driven by our analytical capabilities, which continue to improve by leaps and bounds. You know, those of us who have to interpret data, you know, we need to send a little valentine to the analytical chemist and say take a lunch break, because we can't -- we don't know what to do with what you're telling us anymore.

And so, you know, that's -- I mean, I think that's a huge issue when you talk about those sorts of interpretations.

DR. BARR: That's true.

MS. HOOVER: Gina.

DR. AYLWARD: Absolutely.

DR. KYLE: So I'm not sure -- so --

DR. AYLWARD: Well, and that's actually one of the things when we talk about the Biomonitoring Equivalents that we're working on. One of the things, the analysis we have -- it's actually in publication right now -- is looking at the detection limits. So NHANES measured 40 VOCs in blood samples in the United States. And for the vast majority of those VOCs, for all except about 7 or 8 of them, they basically had no detections in the population.

And so one thing that you might ask is -- the first response might be, Ben Blunt you need to go back and improve your detection limits on your VOC analyses. And you may well want to do that.

But another question to ask is well, were those detection limits of interest in the context of our existing risk assessment. In other words, were his detection limits sufficiently sensitive to provide -- to measure concentrations that we would have been interested in in the Biomonitoring Equivalent sense with respect to our current risk assessments for those compounds.

And so what we were able to do is compare those estimated internal blood concentrations to the detection limits and say that for many of the VOCs the detection

limits were 10 to 100 fold below levels, for instance, associated with the reference concentration.

And maybe that's not as good as you want in a multiple chemical situation, but it does provide some information about that sensitivity and give you some information about what you're not seeing, as well as what you're seeing.

MS. HOOVER: Gina.

DR. SOLOMON: With regard to the question about mixtures. I'm not sure that mixtures really affect where we'd be going, in terms of interpretation, or the information -- or whether the toxicity information that we have about the endpoints that are affected would particularly influence anything in the Biomonitoring Program.

But I actually would instead submit that turning it around could be very informative in taking a look at what chemicals are co-occurring in the population that we're studying, and then starting to look at what the health effects of those co-occurrences might be.

So it's sort of not starting with the a priori, okay, let's look at all the thyroid disruptors, but instead saying, okay, let's look at what's -- you know, sort of do some statistical analyses about what things are co-occurring at sort of elevated levels in various

participants. And then trying to figure out how we would tackle looking at those -- you know, the cumulative health risks of those.

Not necessarily through using Biomonitoring Equivalents, but rather, you know, just sort of, you know, what do we know about those chemicals? And maybe should we be running them together through some of these high throughput screens to see whether they have any kind of effect as a group? Let's take the California mix that we're seeing and, you know, run it through ToxCast and...

DR. BAHADORI: Gina, NTP just put out their whatever common requests for input on their mixtures research program. So that's actually a very good idea. You might want to put that in.

MS. HOOVER: Okay, so we're just going to start wrapping up, so -- Lauren.

DR. ZEISE: Yeah, one real quick follow up on this is of course the problem is that with the pathway kind of testing, you're only testing up one pathway. And the conundrum is that we have these multiple pathways involved with these different chemicals that are leading to greater sensitivity for the individual chemical showing up, if it's in that mixture. And essentially we're exposed, of course, to a wide range of chemicals. And so it's unclear to me how you would perform a high throughput

test of that problem.

DR. BAHADORI: Well, you would do -- put it through multiple assays, the same way that you look at the different pathways now.

DR. ZEISE: So the question is how do you combine?

DR. BAHADORI: Well, but that's what Gina is saying, you can statistically see -- and Mike Tornero from NERL did an analysis of this in the environment. It wasn't in the humans. But he looked at co-occurrence, how -- there is, in fact, not an infinite combination. There is a finite combination in which mixtures occur in the environment. And he draws upon some ecological models. Keith Solomon verified this in his studies as well.

So the story is complicated, but not as complicated as we're all afraid that it is. That there is a pattern in which these mixtures occur in the environment. And maybe from that, we can extrapolate how exposures occur.

And so it's a starting point. So if you look at those co-occurrences and start seeing how something like ToxCast or -- not even ToxCast, but maybe some of the lower throughput -- the medium throughput, lower throughput. The researchy stuff can be, you know,

applied, you know, under -- Andreas Kortenkamp did some of that. First, he did it with the traditional tox studies. And then he did it a little bit with the molecular assay, the in vitro studies. I mean, there are people already trying this.

DR. ZEISE: I think that would be an avenue with the more -- maybe with the more mid-range, in terms of throughput rather than the --

DR. BAHADORI: Yeah, not the high throughput, but the researchy things.

MS. HOOVER: And so Ruthann, I know you had one. Do you have on last short comment?

MS. RUDEL: This is very short and just related, because it's apropos to mixtures, which is just in our California indoor and outdoor air from Richmond and Bolinas paper that was out ES&T this past summer 2010. In the supplemental info, we have a big correlation matrix of all of the chemicals across with all of the other chemicals, both indoors and outdoors. And it does, you know, provide some interesting insights. Like, for example, nonylphenol correlated with the phthalates and some other, but not with the ethoxylates.

So it's not really coming from the APEOs anymore. It's coming from other uses of nonylphenol so, as an example. But we also did urine -- you know, urine

phthalates and found that the urine levels of most of the phthalate metabolites were correlated with air and dust of the parent compounds, but almost as strongly correlated with air and dust concentrations of other endocrine disruptors, like nonylphenol or paraben. So that provides some more information about that along those lines.

MS. HOOVER: Okay. I just want to close here and again thank all of our speakers and the audience. This has been really really helpful. So thank you again for coming.

(Applause.)

(Thereupon the California Environmental Contaminant Biomonitoring Program workshop adjourned at 5:08 p.m.)

CERTIFICATE OF REPORTER

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

That I am a disinterested person herein; that the foregoing California Environmental Contamination Biomonitoring Program workshop was reported in shorthand by me, James F. Peters, a Certified Shorthand Reporter of the State of California, and thereafter transcribed under my direction, by computer-assisted transcription.

I further certify that I am not of counsel or attorney for any of the parties to said workshop nor in any way interested in the outcome of said workshop.

IN WITNESS WHEREOF, I have hereunto set my hand this 28th day of March, 2011.

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