MEETING

STATE OF CALIFORNIA

ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

ENVIRONMENTAL CONTAMINANT BIOMONITORING PROGRAM

SCIENTIFIC GUIDANCE PANEL

THE CALIFORNIA ENDOWMENT

OAKLAND CONFERENCE CENTER

7TH FLOOR

1111 BROADWAY

OAKLAND, CALIFORNIA

THURSDAY, MARCH 27, 2014

10:00 A.M.

JAMES F. PETERS, CSR, RPR
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A P P E A R A N C E S

PANEL MEMBERS:

Asa Bradman, Acting Chairperson, M.S., Ph.D.

Carl Cranor, Ph.D., M.S.L.

Oliver Fiehn, M.S., Ph.D.

Marion Kavanaugh-Lynch, M.D., M.P.H.

Julia Quint, Ph.D.

Penelope (Jenny) Quintana, Ph.D., M.P.H.

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY:

Dr. Gina Solomon, Deputy Secretary, Science and Health

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT:

Dr. George Alexeeff, Director

Dr. Lauren Zeise, Deputy Director, Scientific Affairs

Ms. Amy Dunn, Research Scientist III, Safer Alternatives Assessment and Biomonitoring Section

Ms. Sara Hoover, Chief, Safer Alternatives Assessment and Biomonitoring Section

Ms. Fran Kammerer, Staff Counsel

Dr. Laurel Plummer, Associate Toxicologist, Safer Alternatives Assessment and Biomonitoring Section

A P P E A R A N C E S C O N T I N U E D

DEPARTMENT OF PUBLIC HEALTH:

Dr. Michael J. DiBartolomeis, Chief, Exposure Assessment Section, Environmental Health Investigations Branch

Dr. Laura Fenster, Research Scientist

Dr. Ryszard Gajek, Supervisor, Biochemistry Inorganic Group, Environmental Health Laboratory

Dr. Jianwen She, Chief, Biochemistry Section, Environmental Health Laboratory

DEPARTMENT OF TOXIC SUBSTANCES CONTROL:

Dr. Myrto Petreas, Chief, Environmental Chemistry Branch

ALSO PRESENT:

Ms. Nancy Buermeyer, Breast Cancer Fund

Dr. Veena Singla, Natural Resources Defense Council

Dr. Jon Sobus, Environmental Protection Agency, National Exposure Research Laboratory

I N D E X

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

P R O C E E D I N G S

ACTING CHAIRPERSON BRADMAN: If everybody could sit down. I think we're going to get started now. It's about 10:00 o'clock.

DIRECTOR ALEXEEFF: Good morning, everyone. I'm George Alexeeff, Director of the Office of Environmental Health Hazard Assessment in the California Environmental Protection Agency. I want to welcome everyone here. I want to welcome the Panel for taking time out of their very busy schedules to help us in California in this Biomonitoring Program. I want to thank everyone for attending here in person.

And I do want to let everybody know that this meeting is being transcribed, and it's also being webcast. So when we speak, we do need to speak in the microphones. Even if people close by can hear us, we want to make sure that it's recorded properly.

The first piece of business is I wanted to -- I don't think Michael Wilson is here, is he?

No, I don't see him. Okay. I wanted to acknowledge and thank Dr. Michael Wilson for his service as a member of the Scientific Guidance Panel. Dr. Wilson was a member of the Panel since its inception in 2007, when he was appointed by Speaker of Assembly John Pérez. His dedication was quite evident through his consistent

attendance, enthusiastic participation at the SGP meetings. And also I really appreciated the stories he had about occupational exposure incidents and how that played into biomonitoring.

The Biomonitoring California has greatly benefited from Dr. Wilson's unique perspective stemming from his personal and professional commitment to protecting workers from hazardous chemical exposures. Dr. Wilson's particular attention to worker health and safety issues served to emphasize the importance of addressing occupational exposures in this program. And California is truly fortunate to have expert scientists like Dr. Wilson with a strong commitment to improving public and environmental health in the State.

Now, we are fortunate in the State, Dr. Wilson is now serving as Chief Scientist for the Department of Industrial Relations. So Dr. Wilson is supporting Director Christine Baker in a range of Department of Industrial Relation activities, including the Interagency Refinery Task Force, where he's working alongside Dr. Gina Solomon, another former Scientific Guidance Panel member, who is now Deputy Director for Science and Health at the California EPA.

So I just wanted to give a quick overview of the last week's meeting. At our last Scientific Guidance

Panel meeting was held on -- in Sacramento on November 10th, in 2013. At that meeting, the Panel heard about program and laboratory updates. They unanimously voted to recommend adding two classes of aroma chemicals, synthetic polycyclic musks, and tetramethyl acetyloctahydronaphthalenes to a list of designated chemicals for Biomonitoring California.

We heard a presentation from the Scientific Guidance Panel Member Dr. Oliver Fiehn on identifying novel compounds in untargeted metabolomic screens. And we discussed the next steps for the Program in development of non-targeted screening methods.

And for more information on the November meeting, please visit the Biomonitoring website, which is BiomonitoringCalifornia.gov.

So here in this room in terms of emergencies and look around for the exits, there's one on this side and there's one in which the one we probably most of us came in, just to be aware of that. And I think, at this point, I will turn the meeting over to our Acting Chair Dr. Asa Bradman.

ACTING CHAIRPERSON BRADMAN: Thank you. I want to welcome everybody here to today's meeting, both Panel members and State staff and members of the public. Today, I want to mention that we have a pretty full schedule, so

it's going to be important to stick to our time allotments and I'll remind people if we're encroaching on those.

So just to over -- give you an overview of what we're going to be covering today. We're going to -- the goals today are to -- we're going to have a Program and laboratory update, and an opportunity to provide input on the Program. We'll also be considering chromium as a potential designated chemical. And then we're also going to be considering other designated metals as potential priority metals for the Biomonitoring Program. Finally, we'll be hearing a presentation from Dr. Jon Sobus of the U.S. EPA on best practices for biomarker collection, analysis, and interpretation.

And those of you who have been able to see the presentation online before the meeting today, I think that will be a very interesting afternoon discussion this afternoon.

For each agenda topic, time is provided for Panel questions, public comment, and Panel discussion and recommendations. So the format today will be very similar to previous meetings.

In terms of public comment, if a member of the public would like to make a comment, he or she should fill out a comment card, which can be obtained from the table near the door. You can turn the cards in to Amy Dunn.

And, Amy, if you could identify yourself.

Members of the public who are not at the meeting in person are invited to provide comments via email. Biomonitoring California staff will provide emailed comments to me, so that they can be read aloud during the meeting.

To ensure that the meeting proceeds on schedule and that all commenters have the opportunity to speak, public comments will be timed and will be subject to time limits. And we'll take the available time and divide it by the number of commenters to figure out how much each person can speak in terms of time.

Please keep comments focused on the agenda topics presented. At the end of the day, we'll have an open comment period where any other issues covered can be addressed in your comments.

I want to remind everyone to speak directly into the microphone and to introduce yourself before speaking. This is for the benefit of the people participating via the webcast and also for the transcriber.

The materials for the meeting were provided to Panel members and posted on the Biomonitoring California website prior to the meeting today. There's a small number of copies of the presentations and documents. And there's one sample folder, if you want to see all the

materials that we received for viewing at the back of the table -- back of the room.

We'll take two breaks today, one around noon for lunch, another around 2:45 p.m. I want to mention that our lunch break is a little bit shorter than normal, so don't plan for a long sit-down lunch today.

And finally, I want to introduce our next two presenters, Dr. Michael DiBartolomeis, Chief of the Exposure Assessment Section of the California Department Public Health, and Lead of Biomonitoring California. Dr. DiBartolomeis will provide an update on Biomonitoring California activities. And then following that, Amy Dunn with the Office of Environmental Health Hazard Assessment will give a demonstration of the new results database, which will be launched on the Biomonitoring California website next month.

So thank you, Dr. DiBartolomeis.

(Thereupon an overhead presentation was presented as follows.)

DR. DiBARTOLOMEIS: Thank you, Dr. Bradman, and good morning. I trust everyone has had a happy and healthy and productive break from four months ago. So we're -- I know biomonitoring has made some productive -- some production and progress, so I'm going to cover some of that.

So I have some announcements, a little bit of update on some general Program news, and then some specific project news. And then we're also going to hear -- actually let me change this.

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DR. DiBARTOLOMEIS: We're actually going to hear today a little bit more about our new collaboration, which is new in quotes, because you've heard about the Genetic Disease Screening Program before, but we've made significant progress in moving that collaboration forward.

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DR. DiBARTOLOMEIS: So top on the list is that we have a new supervisor, new staff person, new expert in our program, Dr. Nerissa Wu. Back of the room. So welcome her. And you are going to hear from her right after I finish my piece. She's going to talk about the Genetic Disease Screening Program work.

I want to just mention the legislative report, which is mandated every two years. And there was one due -- the third report actually was due in January is in the final stages of review in the Department of Public Health. It's gone back and forth a little bit, but we're expecting that to be going out in about the next couple weeks. So without getting into the content of it, it's what you would expect having looked at the previous

reports. Although, it's a lot more streamlined, and we think a little bit easier to read. And hopefully, there will be more readership of it.

Secondly, in terms of the Program evaluation -- actually, I'm going to have to put my glasses on. You will recall that it's actually required as part of the CDC cooperative agreement. And we have taken it a little bit step further, where we want to evaluate more parts of the Program for our future improvements and, you know, working off of what has been very valuable to do in the past.

The Program evaluation has actually been spear-headed by Christine Arnesen, and I'm -- oh, there she is. So Christine is here. And we also have a subcontractor helping out on the lab side. And the -- it is well along in terms of the evaluation of the laboratory and the Program. In fact, we're now in the survey place, where we're actually sending out surveys to staff and you -- and for external input as well. And there's a little bit -- you will be hearing a little bit about that in the near future as Christine and Sara will be contacting each of the SGP members or the SGP members about further evaluation.

There have been interviews already of staff. I've been interviewed and I know a few others have. And this is going to be ongoing, but it's actually in very --

it's in very full force right now.

And then finally, back in November, we didn't know for sure whether there was going to be another funding announcement from CDC. Although we're pretty confident that there would be. It has come out. It came out in February. And it's a fairly fast turn around, although better than normal. The applications are due in May, first week in May. We did submit our letter of intent to apply.

In terms of the actual grant opportunity itself, it is for five years, for a maximum of $1 million per year and a minimum of $500,000 per year. And this is significantly less than where we are now at 2.65 million per year. So that -- I'll let you kind of think about that a little bit.

We anticipate that about five states will be awarded the $1 million per year. Since they have five million in there and it's -- they are -- their expectation is the average will be one million per year as an award. They are not going to be awarding more than a million. It's kind of a funny math problem. So you figure that there's going to be about five states. There could be -- if they -- if there's -- there could be six or seven, if some the states take less.

There is -- there are opportunities for

collaborations among the states, but because of the time frame that they give, it's really difficult to really set something like that up. But there are some consortia -- the western consortia for example, consortium, that they may go in as a group. We don't know.

So we are going to be applying, and we are also, in addition, pursuing other funding opportunities. We are looking into -- for example, there's an NIH R01 that we're thinking about -- we're seriously thinking about applying for. It's a community partnership, so it's a little bit different than something we've done in the past. It wouldn't be an academic partnership.

And finally, even though, we certainly gave our kudos to Dr. Lipsett at the last meeting, and I think any time -- I think right around at the time he announced his retirement, we were doing tributes, et cetera, I do want to say that he's actually back, not as a full-blown manager or staff person, but he came back -- he's back as a retired annuitant, at least for the next couple of months. It's unclear what's going to happen after two months. And he has agreed to help out with writing the application for the CDC grant, which is really great for his institutional memory. So we thank him for that.

I also want to thank, by the way -- I should have probably started by saying, we, the Biomonitoring Program,

also want to thank Mike Wilson -- you know, Dr. Wilson for his contributions, which have been excellent and extensive and he will be missed.

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DR. DiBARTOLOMEIS: So in terms of project updates, let's go back to our two friends, the Maternal and Infant Exposure and our Firefighters. I just mainly want to report back that our hydroxy-BDE results have been returned to participants. I think we had projected December back in November, and we were right, and so those are back.

And we have publications in progress. And I'm happy to report that the first publication, which would be the cord and serum blood sample analyses, has been drafted and submitted to the Biomonitoring Program for our input. So our UC collaborators have completed a first draft. And so we are -- so that's really good.

There are other papers that are in the works, but this one we've been wanting to get out the door due to sort of start that domino effect.

And then in terms of FOX, actually there are three publications in progress at different phases. The first paper that we've been talking about for awhile, the PFCs and metals, has been resubmitted -- or soon to be. I don't know if it actually has been. It's going to be

going to the Journal of Occupational and Environmental Medicine. And so we anticipate that should be in press sometime later this year.

And then there is a paper on POPs, which is well underway. It's probably close to being a draft that would be circulated internally for review. And then a third paper on phenols focusing on benzophenone-3 for the firefighters project. I've seen that one. That is a draft well along its way and receiving input. So there are three papers well along their way in terms of publications from FOX.

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DR. DiBARTOLOMEIS: Now, let's turn our attention to the Biomonitoring Exposure Study. You recall back in November we spent a fair amount of time kind of walking through the Pilot BEST and the Expanded BEST.

In terms of Pilot BEST, the Program has completed all the analyses of the chemical panel. So we're done with the analyses. And the second set of results to participants would be going out, we can anticipate, either later this spring or early this summer. And, of course, data will be posted to the website when it's -- when we're -- the results have been returned, just as we have done with other data.

So this is just to give that -- you know, that

matrix table we usually do to give you a sense as to where we are. We are currently still analyzing the actual data itself. And, of course, we're still working on the return packages.

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DR. DiBARTOLOMEIS: And here's just our documentation that our laboratory analysis are completed. So in March we're all complete.

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DR. DiBARTOLOMEIS: In terms of Expanded BEST, I'm also happy to report that we are making headway in terms of starting to analyze the first set of chemicals, and -- even though -- so the sample collections have all been collected, the medical records abstracted, and the data have been entered. So this is now rapidly moving forward. And let's see, the first set of chemicals that will be returned to participants will include PFCs and metals. I don't have a date as to -- projection as to when those will be going out, at least I don't have it in my notes.

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DR. DiBARTOLOMEIS: Just to give you a sense from -- just a -- this is sort of closing the loop from our briefing at the last meeting, we had some target goals for overall participation, and for ethnic -- and

demographics. And I just wanted to kind of give you the final numbers, so you can have a feel for how we matched our targets.

We did pretty well, and we were projecting that. We didn't quite make our four hundred and some total. We were trying to -- we had a target of 450 total participants. We achieved about 341, and -- which is pretty good. Not all the participants that we did have recruited gave -- we were able to use their samples because of different logistic things that happened, like broken tubes, et cetera.

Let's see. From the 248 of those that had viable samples, we selected a subset of 218 who will be analyzed for all the chemical panels. For the subset, we oversampled for Spanish speaking Hispanics and Asian and Pacific Islanders.

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DR. DiBARTOLOMEIS: And this table is our breakdown of the n's in terms of what our targets were and what our total enrollment was. We pretty closely matched our goal of hitting a 50/50 on the genders. Typical of these kinds of things, men don't tend to show up as much. I guess we're scared of needles.

(Laughter.)

DR. DiBARTOLOMEIS: I'm not exactly sure what

else is -- what other reasons. So, let's see, and the -- this is interesting, the total enrolled mean age was 48, and the sample mean age is 49. And if you recall from Pilot BEST, it was significantly higher. I think it was 55, something like that.

So we did -- we did -- our target was to have a younger age group. And so apparently our methodology at least did accomplish that. Okay. Well, I'm going to be available for questions, but I want to turn now and yield the rest of my time to Dr. Wu, who will come up here.

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DR. DiBARTOLOMEIS: Who's shadow is -- no -- who will be covering the next couple of slides and the Genetic Disease Screening Program collaboration.

DR. WU: All right. Good morning. I'm going to just spend a few minutes talking about the Genetic Disease Screening Program which oversees the California Biobank, the repository of screening samples, since Biobank may play a significant role in biomonitoring in the next few years.

So GDSP, or Genetic Disease Screening Program, is part of the Department of California -- the California Department of Public Health and they offer prenatal screening and newborn screening across the State. By law, prenatal screening is offered to all pregnant women as

they walk in and access prenatal care. And about 70 percent of women, or about 350,000 cases, annually opt for screening.

At the time of screening, patients are consented for screening, but there's also a little message on the consent form that says your sample may be used for future departmental research, and there is an opt-out check box, but very few patients, about five percent, opt-out of this.

Patients are also asked for some demographic information, their age at term, maternal race, maternal weight. These are things that are used for the risk assessment for the outcomes of the Genetic Disease Screening Program.

And then after screening is completed, the samples from the seven counties listed, the counties that are involved with the birth monitoring registry, they are stored in the Biobank. Newborn screening similarly is offered statewide to all women. About 90 percent of women take us up on the screening program. It's a heel stick, and the sample is stored on a blood spot. And again, there's all this patient demographic information that is collected along with some infant information, such as gestational age at delivery, the time and date of delivery, and the time and date of sampling, which is all

key to the risk assessment for GDSP.

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DR. WU: Now, the biobank samples from the seven different counties. And except for the people who have denied consent for research, and people who are in the registry, if they've been identified as positive for one of the genetic diseases, these samples are all held in this repository and made available to researchers.

This is an enormous resource that Biomonitoring hopes to make use of. There is a cost for the samples. They're $50 per sample, and there's also some analyst time involved. For example, if you wanted to identify a certain subset of samples from a geographic region or certain demographic of patients, there's some analyst time on GDSP's part that we would have to pay for.

They have just opened for business. Their regulations over Biobank are just making their way through the system, but they are prepared -- they are preparing to get prenatal samples distributed as researchers get in the queue. So we have a plan, through our current CDC grant, to access about 450 samples in somewhat of a pilot study.

The plan is to get these samples and do some analysis for persistent organics, PFCs, and metals. We have gotten through the -- we have submitted to the IRB. We hope to hear back from them in the next couple of

weeks. And then we'll be getting in line with other researchers in hopes that GDSP will get us these samples within the next month or two.

So this is potentially a huge resource for biomonitoring. It's true that it's not fully statewide. Although, there is the potential for Biobank to work with us to expand their geographic reach. And, yes, it's only women who are pregnant, but it is a wide swath of the California population accessing people that we just don't have that kind of ability to get that range of samples through our studies.

And it could help us focus future studies. For example, if we see some results that indicate that focusing on a particular ethnic community or geographic region, that will really help to focus our future research.

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DR. WU: I just want -- I'll finish up with the slides. I just want to thank and acknowledge all the Biomonitoring staff. I'm a recent addition to the staff.

Thank you to the whole staff. It's been impressive. The people that I'm starting to work with are --

(Thereupon phone interference occurred.)

DR. WU: Can you mute your phone, please.

Hello.

And to echo Michael, I just want to thank and acknowledge Michael Lipsett. Congratulations on his retirement. He has been spotted in our office, but we have heard rumor that he is also enjoying his retirement and his new careers.

(Laughter.)

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MS. DUNN: So just quickly, I'm going --

(Thereupon phone interference occurred.)

MS. DUNN: Can you hear us whoever is talking? We are hearing you, and we need you to mute your telephone?

Okay. So we're just going to give you a quick overview of one of the projects that we've been working on since the biomonitoring website launched in July, and that is our results database. We've also been working on some other projects, including some new content in Spanish, which we're excited about, and we'll tell you about in another meeting.

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MS. DUNN: So Laurel and I have been working together to create a results database. Now, we have an existing structure that's shown here on the top right-hand side of this slide, which is pretty basic that involved

tables posted by each chemical class for each project. And the challenge for us has been that each time we needed to update something, we had to upload again. And each time --

(Thereupon phone interference occurred.)

MS. DUNN: I'm sorry. Can you stop right now? You're interrupting the presentation, and so --

(Thereupon phone interference occurred.)

ACTING CHAIRPERSON BRADMAN: I don't think they can hear us. Do we have a technical liaison here?

DR. PLUMMER: Yeah, he's on it.

(Thereupon phone interference occurred.)

(Laughter.)

ACTING CHAIRPERSON BRADMAN: Just to explain to our webcast listeners, we're having some -- we're hearing in on a conversation from somebody else that's coming in over our speakers. We're trying to get that resolved.

MS. DUNN: Okay. So anyway, we have developed a new approach that we feel is going to be much better for both the staff and also for those who are interested in looking at our information.

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MS. DUNN: Some of the elements of the new results database are that you can climb into the data either by project or by chemical group. You're going to

be able to filter, so that you're looking at just what it is that you're interested in, and there's also easy ways to get additional information on chemicals, projects, and the terms that are used in the tables. And the same kinds of statistics as we've been providing is what we'll be providing in the new database.

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MS. DUNN: We're very close to launch. We're hoping to launch in April. We're just fine-tuning some of the navigation, doing a final review of the data, and finalizing some other -- the supporting content. And we'll be announcing about the database launch to our listserv and also to others, and we're interested in your ideas about how else we might want to get the word out to people. And we are also hoping to add some additional features post launch.

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MS. DUNN: I want to shout out a big thank you to our web developer Uli Weeren at Studio Weeren, and also to the Centers for Disease Control for some of our funding.

(Thereupon phone interference occurred.)

MS. DUNN: Let's see.

So this is the view of our existing -- or of our new results database in a draft form, but this is pretty much what it's going to look like, except for the pink

across the top. And as you can see, there's two columns, the project or chemical. And you can climb in either way. Both have the same information. And here I'm just going to briefly show you -- because we're short on time, I'm going to show you, for example, if you climb in via the chemical group environmental phenols, you can see the tables for the two projects that currently have results for this chemical group.

And this is a link to more information about this project and these are links to more information about these chemicals.

Now, another feature that we think people are going to like is that you can filter the results. So, for example, if you were only interested in the bisphenol A results, you can filter it like that. And one of the things -- you know, in this case, there's not that much content, so it's not -- you know, you can look at the whole table, but eventually we're -- you know, we'll have a large list of projects, and this will make it much easier for people to get this kind of information. And this kind of filtered information will also be accessible via the page for each chemical that's been measured.

So here you can see this little box of results is going to take you through the same kind of page as what we just saw by filtering in the database. So I know we're a

little short on time, so I'm not sure if I should try to wrap it up.

ACTING CHAIRPERSON BRADMAN: We're actually -- we're doing okay, if you want to spend a few more minutes.

MS. DUNN: We're doing okay. Okay. So just to give you a little bit of a different view in, so if you come in, for example, through the project-related content, you'll see everything that's been measured for the California Teachers Study all provided in -- you know, in one table. And this is going to grow for each of the projects as you move forward -- you know, as the Program moves forward with more samples.

Now, one of the other things that I didn't mention earlier is that it's also possible in the database to export the values in the table as an Excel file, so that if people want to use the information in that form and manipulate it themselves, that's going to be possible, and also to print it as it appears on the table.

This is one of the things that we're going to be working on as we go forward, because right now it's not possible to actually print or capture the filtered results, but that will be coming. So I guess, at this point, I'm just going to turn it back to the Panel and, you know, Laurel and I would be glad to answer any questions.

ACTING CHAIRPERSON BRADMAN: Okay. Thank you. Just members of the Panel, we now have about 10 minutes, maybe a little bit more -- we're doing pretty good on time -- for any questions to the Program staff on today's updates, anything related to what's already been presented today.

Oliver.

PANEL MEMBER FIEHN: Okay. I have a loud feedback.

Okay. I have a question on the Biobank process in terms of sample storage, how samples are prioritized, because it's obviously valuable, you know, samples. So I see here on the photo, a tube that may contain 10 milliliters of -- you know, it looks like an EDTA tube, but I'm not sure. So, you know, about freeze thaw cycles and so on. So how does this process work?

DR. WU: Okay. Well, there's several questions. So let me see if I can answer them in order. In terms of prioritization, you do not get into the queue until you've completed all of the process getting registered with the GDSP and getting your IRB approval. So we're actually not even in the queue yet, but other researchers are in the same boat, by which they need to go through that whole complete IRB.

PANEL MEMBER FIEHN: Of course.

DR. WU: It's just -- it's really a first come first serve, unless you are working with GDSP on a related project, a project related to their outcomes, in which case you have some priority. So it really just matters -- it really just depends on how organized other researchers are.

In terms of that picture with 10 ml, that's not a picture of an actual Biobank sample. They collect very little. And one of the difficulties with doing these biobank samples is that there's sort of an unpredictable volume that's left after screening it. It really depends on how many runs they've needed to do as part of screening.

We are guaranteed at least 1 milliliter. It may be as much as two. We can ask that they give us higher volume samples, but it's a little bit of an eyeball measure. So what we've planned to do with our 450 samples, and again this is a little bit of a pilot to see how it works, we'll divide those up. A third will go to each lab for a panel. And if there's any left-over material, we're planning on taking those, pooling them by demographic and using it for some unknown screening or some additional environmental contaminants that won't be dependent on individual exposure issues.

PANEL MEMBER FIEHN: Thank you.

DR. WU: Was there another? I can't remember if I got everything.

PANEL MEMBER FIEHN: Why type of, you know, freeze thaw cycles, how it's aliquoted, and what kind of sample it is? Like is it EDTA or --

DR. WU: You know actually Jianwen might be able to answer it. I don't know the lab protocol, but do you know, Jianwen?

DR. PETREAS: I can answer that.

Good morning. Myrto Petreas. In the previous meetings, we had presented our pilot -- you have a very good question, because we're concerned about will the samples be amenable to our testing? They're collected for a purpose and they're used in different labs for their purpose, so without thinking about contamination for trace chemicals that we may encounter.

So what he had done a few months ago is working with our Department of Public Health Genetic Disease Laboratory, which acts, I think, as a referee lab for all the conventional clinics that do this work. And we obtained some of their samples, which is -- they have gone through any kind of cycles from different plungers have been placed in them, different autosamplers have been standing out for a long time.

So this was like a snapshot of what could be

expected. We analyzed those samples, and we didn't see anything significant in the background. At the time same, time we had given -- it's also the issue of the tube they were using, so we used -- we did several tests by sharing -- giving them our samples, spiked bovine serum that we know the concentration and asked them to keep them the way they would have done it open for so many hours, and again there was no change.

So we don't know. It was a very small study with one lab. And these samples get treated in different labs, but we felt, you know, the error, the bias could be smaller than anything that we want to see.

So that's -- it was encouraging what we saw so far with that, but -- and we don't know. We cannot control how many freeze/thaw cycles they had done. But once they come to our lab, they go through our protocol, which is only one thawing.

ACTING CHAIRPERSON BRADMAN: Thank you. Question from Dr. Quint.

Oh, okay. Thanks.

DR. SHE: It's possible our lab we use for the metal analysis. So I think it is a very good question beyond what Dr. Myrto said. Stability is the issue. Long-term storage stability we need to evaluate. For example, for the arsenic speciation, we possibly cannot do

with this kind of samples. We are aware beyond the serums, we are looking for the stability for dry blood spots. That's a lot of metrics that face the same issue about sample stability.

ACTING CHAIRPERSON BRADMAN: Dr. Quint, and then Dr. Cranor.

PANEL MEMBER QUINT: Julia Quint. I had a question about the population of women from whom the samples are taken. I know you mentioned certain counties, but is this mandatory testing, so it all women in all hospitals or is it --

DR. WU: Are you referring to prenatal or newborn or both?

PANEL MEMBER QUINT: Prenatal, the pregnant --

DR. WU: Okay. Prenatal. It's mandated that the screening be offered to women when they access prenatal care. About 70 percent of women elect screening, so it is --

PANEL MEMBER QUINT: So all hospitals?

DR. WU: All hospitals, all clinics, all prenatal providers are obligated to at least offer it.

PANEL MEMBER QUINT: Okay. And the newborn is mandatory, so that's --

DR. WU: It is quasi-mandatory. I mean the hospitals, I think, are -- it's again mandated to be

offered and parents can opt-out of it. It's a -- there's a little bit of a process to opt-out of it or to have your newborn card destroyed after screening, but very few people take -- contact the State and ask that that be done.

PANEL MEMBER QUINT: So we're talking about a very diverse population here?

DR. WU: Yes, there's very good coverage. About 90 percent of newborns are screened.

PANEL MEMBER QUINT: Thank you.

ACTING CHAIRPERSON BRADMAN: Dr. Cranor.

PANEL MEMBER CRANOR: Yes, just a quick question, follow up on the genetic screening. So these are both women and newborns that are undergoing screening for genetic issues, but they're sharing the blood for screening for chemicals, is that correct? I don't understand. There's something missing here that I'm -- I missed the November meeting, so maybe you discussed it there.

DR. WU: The prenatal screening is a maternal serum, and they're looking for when they do a whole panel of pregnancy associated hormones and chemicals for trisomy outcomes, and neural tube detects in the infant. It's genetic disease screening on the newborn using maternal serum. The newborn -- the newborn screening is using a

heel stick of the newborn infant in a blood spot.

We are only using the maternal serum for this round of our Biobank draw. We're only taking the prenatal serums.

PANEL MEMBER CRANOR: What I don't understand yet is, is this the typical genetic screening that had been done in the past, and then you're sharing what you get, or is this a new program specifically for screening for chemical substances?

DR. WU: Our use of the samples will be separate from the Genetic Disease Screening Program. They're just -- they just happen to be samples that were collected for the purposes of screening --

PANEL MEMBER CRANOR: Okay. That's what I thought, yeah.

ACTING CHAIRPERSON BRADMAN: Any other questions from the Panel. Okay. I had one question and one comment. The comment is just I'm just very impressed with the database and the new web features. And I think that will be a great addition to the Program, and make it very -- you know, much more accessible both -- to anyone who may use it from the general public, to researchers, to, you know, association or industry folks. I think that was a great contribution.

And then I just had a quick question on metals.

Can you just remind us very quickly, the target analytes for the metals in urine that were measured for the Pilot BEST, and then also I think in blood? Just a quick list.

DR. GAJEK: Ryszard Gajek.

We analyzed for urine in metals, which basically first we included manganese, arsenic, cadmium and mercury. Then we discovered that all our lab were -- is contaminated with manganese, and we had to skip manganese. But pretty much we are now in control and we can include back manganese.

ACTING CHAIRPERSON BRADMAN: Okay. And the blood measurements were?

DR. GAJEK: Oh, so we analyzed except for arsenic, the same.

ACTING CHAIRPERSON BRADMAN: Okay. Thank you. I think that might be relevant to some of the discussions this afternoon.

Are there any more comments or questions from the Panel? This will probably be the last one to stay in time.

PANEL MEMBER QUINT: Julia Quint. I just had a quick question for Dr. DiBartolomeis about the budget. Just a very quick one. I just wanted to be clear. You said that the CDC grant would be a million dollars, but you were operating at 2.6 million is your budget now? I

just --

DR. DiBARTOLOMEIS: You always ask me the easy questions. So actually, the CDC grant right now that ends on August 31st is $2.65 million per year, and this -- we're on the fifth year. So the new FOA funding opportunity is for one million per year we hope for five years, as long as CDC's money doesn't run out.

So the difference so to 2.65 to one million on the CDC grant. We still have State funding. That has not -- it has not changed.

PANEL MEMBER QUINT: Right.

DR. DiBARTOLOMEIS: So overall, the Program has a, you know, much bigger budget than what CDC is. That's their supplement.

PANEL MEMBER QUINT: But you would have to make up the difference with the State budget if you -- I mean, if you only got a $1 million is what my basic question was?

DR. DiBARTOLOMEIS: The best case scenario is we make up the difference with other funding sources.

PANEL MEMBER QUINT: Got it.

DR. DiBARTOLOMEIS: The worst case scenario, which we are planning for, is to reduce our staffing and production.

PANEL MEMBER QUINT: Okay. Thanks.

ACTING CHAIRPERSON BRADMAN: I think that completes our Panel questions right now. I want to mention again to the people on the webcast, we seem to be having an ongoing problem, where somebody else's voice is getting picked up on the PA system, and we're trying to address that. But if you hear some errant conversation that don't seem related to this meeting, they're not.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: And people are trying to work on that.

So now we have an opportunity for public comment. We have 10 minutes designated here right now. We just have one participant who's asked to make public comments. That's Veena Singla from the Natural Resources Defense Council.

So thank you.

DR. SINGLA: Thank you. I had two questions. First, I wanted to comment that it's great --

ACTING CHAIRPERSON BRADMAN: Is your microphone on?

DR. SINGLA: It's great to hear that there's publications to be coming out soon from the Program work. And I wondered if there were plans, in addition to when these publications do come out, to have them brought to the attention of a wider audience, perhaps through media

releases, especially in California. I think it would be important to bring this to the attention of the general public and a wider audience, the publications that are coming out of this program the results that they're finding and to be able to put that information in a more understandable form for the general public.

And my second comment and question related to the results database, I agree with Dr. Bradman that it's great to have this kind of more streamlined and easily accessible forum to see the data. And I wondered if there was anyway there to provide more context as well in the summary tables, something to make it a little more informative for a wider audience? I don't know if there's some sort of relevant comparison that could be provided, maybe to NHANES data or to previous data from the Program, just to give a little bit more context to those numbers?

ACTING CHAIRPERSON BRADMAN: So we're actually running ahead of schedule, so if -- feel free to be verbose.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: We have about 10 minutes now designated for some additional Panel discussion. I want to respond briefly to the public comment we just had, and maybe one suggestion to look at for providing some interpretation is the Department of

Pesticide Regulation website, where they have kind of some analyses related to the Pesticide Use Reporting data. And they periodically will publish, you know, evaluations of the PUR data and post that, along with other information, along with a lot of detailed information.

Those evaluations tend to assess trends in use and things like that. And I think similarly, the Biomonitoring Program could assess trends, make comparisons, and things like that, usually in a narrative format. Although, the PUR information tends to be dense with words. Maybe something more visual and in summary fact sheet fashion might be more accessible.

So we have more opportunity now for the Panel for discussion related to the last session.

Dr. Fiehn.

PANEL MEMBER FIEHN: I also would like to comment that I very much applaud the results database, the progress that's been made. I couldn't really see it very well. So, you know, can you just comment quickly on whether all the results are displayed as individual by person results or as accumulated averages and means and deviations for the individual compounds. I couldn't really see that very well.

MS. DUNN: Yes. I'm sorry that the visibility was poor. They are summary statistics, so no individual

data are being provided. So this is the same data that -- I mean, the same type of information that's in the tables that we're posting currently. So we're not actually changing the kind of information, just the way that we're presenting it. I mean, the way in the sense of like how you can get at it.

PANEL MEMBER FIEHN: And what is the reasoning behind these kinds of summarized tables instead of individual samples, so to say, is there any confidentiality issues or --

MS. DUNN: Yes.

(Laughter.)

MS. DUNN: I forgot with the interruptions that were a little distracting, that Laurel has offered to give people a more personalized tour of the database during the web -- I mean, during the lunch hour for people who are interested, if you want to come back 15 minutes early from lunch. It might be challenging to do that, given our short time, but if you're interested, or you can wait a couple weeks and you'll have a chance to play with it.

ACTING CHAIRPERSON BRADMAN: Dr. Quint.

PANEL MEMBER QUINT: Julia Quint. I had a similar question about particular analytes or chemicals. I think you can -- right now, you can just access a chemical and look at the results across all studies, is

that correct?

DR. PLUMMER: Yes, that's a feature of the filtering at the top. So depending on what you're interested in, you can choose from the check boxes of a chemical group or a specific chemical, which Amy demoed that on BPA.

PANEL MEMBER QUINT: Right. So you can compare with different studies what results you got for the same chemical?

DR. PLUMMER: Yes.

PANEL MEMBER QUINT: Great.

ACTING CHAIRPERSON BRADMAN: Are there any more Panel discussion or questions or recommendations related to the previous agenda item?

Dr. Quintana.

PANEL MEMBER QUINTANA: Hi. Jenny Quintana. I was wondering if the database linked to the information as it was presented to participants, like in the example of here's how this would be given to the participants which might be a more friendly format, in terms of interpreting the data? Is that linked or on the website available or plan to be available?

MS. DUNN: So the information that we provide to participants, which is currently on the website are the fact sheets. So the chemical-specific fact sheets. And

those are -- so I know it was hard to see, but the right hand -- I mean, the left-hand column of the table where the chemical name is, that links to the chemical page, and that's where the fact sheets are also reached via that page.

DR. PLUMMER: Just really quickly. So each participant gets their individual results. And I think -- Duyen, correct me if I'm wrong, but -- and they're compared to a comparable NHANES group. And so at this stage, we're not doing that in our data, because I think once our publications come out, that's a feature that, you know, would be great to include.

ACTING CHAIRPERSON BRADMAN: Dr. Kavanaugh-Lynch.

PANEL MEMBER KAVANAUGH-LYNCH: Hi. Mel Kavanaugh-Lynch. I've been turning this idea about the Genetic Database Program -- or, sorry, Genetic Disease Screening Program. So I understand it's a State program that was put in place by legislation presumably. And I -- here's my thinking. The Biomonitoring Program was also a State program that was put in place by legislation, so the fact that we get thrown -- we -- the Biomonitoring Program gets thrown in with all other interested researchers has to go through an IRB, has to wait, get -- wait in line, has to be prioritized, et cetera, and then has to pay $50 per sample seems not the most efficient.

I understand it's the process they now have. My question is, is there a place here for advocacy or for some movement where we could suggest an amendment to the legislation for the Genetic Disease Screening Program that then requires them to give the Biomonitoring Program their samples when they're done with them and at no charge, and let us do what we -- what the program feels is best to do with them?

Because I know the Biomonitoring legislation required a, you know, community based, statewide sampling, and here is a program that albeit only -- is limited to only women and only those who are child-bearing age, and -- et cetera. It's still as close as we're going to get in the current budget climate to anything like the biomonitoring legislation requires. And this would be, I think, a great example of how this State could help the State.

DR. DiBARTOLOMEIS: So that's a very astute and very good question, in terms of whole management of this. Let me take a crack at this, and -- one of the things I didn't do was tell you that Dr. Wu, who is previous -- most previously of the Safe Cosmetics Program. Before that, she's with the Genetic Disease Screening Program. So she actually has intimacy of the program that I would never have. But what I understand from meeting with the

folks at GDSP is that, first of all, what's sort of held the process up at this point above being able to share these samples with researchers has been that they've had to promulgate regulation. And in that regulation, I believe, is where the pay for sample comes up.

DR. WU: They need to be able to support their program.

DR. DiBARTOLOMEIS: Right. So they're supporting the program through the fees that they would generate from being able to share these Biobank samples to researchers. Now, your question though is more in line of, well, you're a State program and they're a State program -- in fact, you're just across the street from each other -- why are you paying and whatever? Again, this has been a decision by the CDPH management that they -- that even though we are sister programs, that unless we are actually working on a joint project with -- you know, in collaboration with the Genetic Disease Screening Program, which we are not right now, we would be subject to having to pay the fees as well.

In terms of prioritization, on the public surface, we are not going to be treated any differently. However, they are intrigued by the opportunity to be working closely with the Biomonitoring Program knowing that we are in the same department, and thus -- so they're

eager to have us do this. And I think that we might be able to push things a little bit faster, if that makes any -- I'm trying to be somewhat diplomatic here.

In terms of legislation, boy, if -- you know, legislation is great. It can change many laws, and you can have all kinds of things happen. I just can't comment on that. I mean, just, quite frankly, that's just not something I can comment on.

But, you know, if there were -- if there was legislation that created a relationship between Biomonitoring and GDSP in terms of sharing samples, you know, mechanistically, that could facilitate the Program getting samples at a cheaper cost.

ACTING CHAIRPERSON BRADMAN: Other questions?

I have a question for Dr. Kavanaugh-Lynch. I kind of heard in there a recommendation. And I wondered do you want to make a specific recommendation as part of this time right now? We have an opportunity to do that, and something that the Panel as a group may want to put forward?

PANEL MEMBER KAVANAUGH-LYNCH: I'm not sure what we're allowed to recommend as a Panel that advises the Biomonitoring Program. And so, yes, I would like to make a recommendation that goes as far as I'm allowed to go.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: Well, you know, I --

PANEL MEMBER KAVANAUGH-LYNCH: Those who are in the audience who may be from advocacy organizations that do work in the policy arena perhaps can go further.

ACTING CHAIRPERSON BRADMAN: Right. I mean, my understanding is where we make formal votes for designating chemicals, that has, you know, a specific and circumscribed process. But I think as a group, we can have opinions and suggestions on how to advise the State on how to, you know, best meet some of those standards.

And I think what I heard there was that we would recommend closer collaboration between the Biomonitoring Program and the Genetic Disease Branch and suggest that CDPH management come together and try to optimize those resources for the Program.

PANEL MEMBER KAVANAUGH-LYNCH: That's what I want to suggest.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: Does anyone agree or disagree or want to comment on that?

PANEL MEMBER CRANOR: If that were a motion, it sounds like a good idea. I would second it, if that's appropriate.

ACTING CHAIRPERSON BRADMAN: Okay. Well, I'll make a motion that the Scientific Guidance Panel

recommends to the State Genetic Disease Branch and the Biomonitoring Program and the CDPH management, that they evaluate the programs and figure out ways for them to be able to collaborate together in a way that optimizes the scientific resources in the Genetic Disease Branch Biobank and the financial resources to better achieve the goals of the biomonitoring legislation. That's my -- do we need to take a vote on that? How about just aye or nay?

Any ayes?

(Ayes.)

ACTING CHAIRPERSON BRADMAN: Any nays?

Okay. So I think that would constitute then a recommendation from the Panel to further explore that and see if we can improve that relationship.

I think, at this point again, we're a little ahead of schedule, which is great. I know we have a full afternoon. So I want to introduce Dr. Jianwen She, Chief of the Biochemistry Section in the Environmental Health Laboratory Branch. And also Dr. Myrto Petreas, Chief of the Environmental Chemistry Branch in the Environmental Chemistry Laboratory in the Department of Toxic Substances Control. And we'll get an update now on the laboratory activities.

(Thereupon an overhead presentation was presented as follows.)

ACTING CHAIRPERSON BRADMAN: Thank you, Dr. She.

DR. SHE: Thank you, Dr. Bradman. Good morning. Welcome.

MS. HOOVER: This is Sara Hoover of OEHHA. We're just trying to resolve the technical problems on the line, so we're going to do one quick thing before Dr. She starts his presentation.

DR. SHE: Good morning again, and welcome members on the Panel and -- of the Panel and audience. Today, I will provide update for EHL. This includes our recent laboratory collaboration with the University at Berkeley on the HERMOSA Study. Plus, we think an exciting update on our targeted unknown screening. And finally, our future works.

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DR. SHE: This overviews, and I already talk about this.

--o0o--

DR. SHE: HERMOSA Study was designed by our collaborator at UC Berkeley to characterize levels and the source of potential endocrine disruptor chemicals from personal care products in young Latina women, and to lower these exposures by using alternate products. EHL analyzed two groups of chemicals. One group was the phthalate metabolite, and another group is environmental phenols.

Of course, we also analyze creatinine for normalizing data purpose.

Endocrine disruptors are chemicals that act like hormones. They mimic, or block, or otherwise interfere with the hormones in our body. Many of these chemicals are found in makeup, and other personal care products, like toothpaste, perfumes, sun screens, et cetera.

The study was focused on teenage girls, because first they use a lot of these products; and, second, they go through a period of reproductive development and there is not enough research about what this endocrine disrupting exposure might do in the long term.

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DR. SHE: There were 100 teenage girls enrolled. So basically, we analyzed 200 samples. The HERMOSA Study team first catalogued what current personal care products the young girls were using and replaced them with low chemical products for three days.

For example, some of the products they received were shampoo, conditioner, soap, lotion, liquid -- conditioners, and eye-liner and lip stick.

MS. HOOVER: Sorry. This is Sara Hoover again. We are -- we're trying to deal with the caller interrupting the meeting, so we're attempting to mute the lines, but now there's no audio on the webinar. So we're

just going to try one other way. So if you could pause for just one minute.

Okay. This is a test. This is a test. Actually, anybody on the webinar, if you could email the biomonitoring email, and let us know if you can hear this test. We would really appreciate it.

Thank you.

(Thereupon a discussion occurred off the record.)

MS. DUNN: Testing one, two.

MS. HOOVER: Well, ask someone to email here.

Hi. Sara Hoover, OEHHA again. We just unmuted the lines. If you can hear us, please email the biomonitoring line. Thank you.

Okay. Testing, testing. Apologies if anyone can hear us.

(Laughter.)

MS. HOOVER: We're still trying. Testing, testing.

Okay. I am trying again. Can you hear us? Testing, testing.

ACTING CHAIRPERSON BRADMAN: Probably in terms of public participation, the afternoon issues are the most important.

CAL/EPA DEPUTY DIRECTOR SOLOMON: Let's just go ahead.

ACTING CHAIRPERSON BRADMAN: Yeah. So we're going to get started again. Sara, I think we're going to get started again, and maybe we can resolve it at lunch.

MS. HOOVER: Give us one more minute.

ACTING CHAIRPERSON BRADMAN: Okay. We're going to give one more minute. I'm timing.

Forty-five seconds. Anybody want to do some jumping jacks?

MS. HOOVER: Okay.

ACTING CHAIRPERSON BRADMAN: All right. Okay. So we're going to get started again, and we resolve any technical issues at lunch time. And we want to continue Dr. She. Thank you.

DR. SHE: Okay. I will continue from Slide 4. And gladly I have Alanna help me type the script so I can continue again with this interruption.

So I started with slide 4. There were 100 teenage girls enrolled for the HERMOSA Study. And as I mentioned that UC Berkeley team already catalogued the chemicals before the intervention and then give them the chemicals.

The pre-intervention urine was collected on Monday, you can see on the slide. And the girls were instructed to use on the low chemical product given to them. Their post-intervention urine was then collected on

Thursday. EHL measured both sets of chemicals for various phthalates and the environmental phenols.

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DR. SHE: And the next two slides does -- we group the 200 samples together without separating the pre-intervention results from the post-intervention. So this data is less important, just to show you a range. And we hope the UC Berkeley team can look further in the data to show the difference between before and after intervention.

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DR. SHE: Slide 5, on the first column, you can see we measured about 10 metabolites for the phthalates. Due to this collaboration, we were able to expand our panels. We usually, for example, for our other program, we only measure six or seven metabolites. With this collaboration, now we're able to report ten of them. Our focus will be only on the low mEP, mBP, miBP.

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DR. SHE: For the environmental phenol group, we measured the seven of them, which include bisphenol A, BP-3, triclosan and the four parabens.

And the last column and the third column -- the third column show the detection frequency, which is comparable with the CDC's. Also, the LOD on the second

column very comparable to CDC method. And the final column shows the range. But again, the -- we are looking forward to updating you with more breakdown results in the future report.

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DR. SHE: At this time, I'd like to thank our collaborator Dr. Kim Harley, and Dr. Kimberly Parra and Dr. Asa Bradman from UC Berkeley team was also the other members from CHAMACOS communities, and Ms. Jose Camacho and other team members for HERMOSA.

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DR. SHE: Now, I'd like to change my topic a little bit. And we mentioned in August meeting 2013, our laboratory already purchased a high resolution accurate mass machine, which is Exactive Plus. And in the last few months, we get it installed. And then we are very excited that we're able to get some results, and then we're able to put in for this report.

So the picture here shows you Exactive Plus machine. The machine's feature have a very high resolution. It's possibly one of the highest resolutions, so it will give you like a 140,000 resolutions. The resolution higher means that we can see the small difference between the molecular, so that we generally think this way.

Also, we like to have very high sensitivity, because the machine for environmental extraneous compound in our bodies the level is not so high. So we do need to have a very high sensitivity machine at least to see them. So this machine is very sensitive. You can see the femtogram that's very, very low levels we can see.

And we also hope this machine can give us the capability to do identification of unknowns at the same time it can do the screening of quantification what we are working on the other chemicals -- some people cause this feature called PAnDA, Post Analytic Data Acquisition, which means we can look back our previous acquired data without doing the experiment. This is another feature the high resolution machine can provide us.

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DR. SHE: Unknown screening strategy. We listen the advice from the group and also talk with other peoples. We think we should start with less ambitious goals. So first, we start with the targeted unknowns, instead of to seek to do unknown unknown. This means we target first the chemicals may have the persistent by a community toxic CTDs, PBT groups of chemicals, which I mentioned in my previous report. We use Derek Muir's database, which includes 600 compounds. Derek Muir work for Environment Canada.

We also look for the European database called SIN List. SIN List also includes many data -- many chemicals related to what we are doing. And, of course, our database covered all of the chemicals we are currently working on.

So which come to my second point of the strategy. Since the database have the chemicals where we use other method of doing, so the second strategy that we treat known compounds as targeted unknowns, which means we validate this machine -- can this machine see the chemical we are already measuring at this moment? So, for example, we include phthalates, phenols, and other chemicals.

And last point is there are many databases available, but what's a relevant database? So we need to better our database. We called TCF, Toxic Chemical Finder. We get all of the data chemicals from their Derek Muir's recommended list, SIN List, our own chemicals. We put about over 600, around 700, compounds into our database, which includes molecular formula, accurate mass, and isotope profile of the chemicals.

And the other strategy we think we -- both laboratories, ECL and EHL, both -- our sister lab and us, we collaborated together. ECL get a different machine, we can cross-validate each other. Also, very luckily, in California, so many expert groups, like UCSF, UC Davis,

Institute of Scripps. They are very experienced in this area. We are very lucky we can collaborate with them.

And the other part that we use our own previous database better experience, which, for example, I mentioned, personally I like the database called ASES, Automatic Structure Elucidation System, which includes 54,000 compounds. We licensed 2,800 compounds to NIST to Dr. Stephen Stein, which is commercially used by people who use GC-MS/EI database. So we build our own -- our own database built it and the library search experience and they're looking for further collaboration to expand this database.

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DR. SHE: We started with the very simple sample clean-up procedure, because we like to see all of the chemicals in the screening process. We do not want to lose them. So this very simple sample clean-up procedure will allow us to do that. So I will not read this and limited by time.

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DR. SHE: As I mentioned, this mass spectra workflow I already mentioned before, is we look at library search. So that's what I mean the targeted unknown. Targeted means it's a compound already in our library. If something not in the library, we are not concerned at

moment we need to develop a new strategy, but first this 700 in our library is our targeted unknowns.

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DR. SHE: From the library search, we have a putative or tentative hit list. This list is based on the criteria matched the exact mass of the molecular in our samples, for example, from urine, with the database chemicals. And also each chemical have I call it a finger print -- a finger print, like they have different isotopes.

For example, if this chemical have a chlorine, you will think chlorine 35 plus chlorine 37. If you have five chlorine, we see six peaks. All these six peaks we have relationship -- quantitative relationship. So from the criteria, accurate mass, and the accurate isotope profile, we can generate this hit list.

So on the bottom, we see triclosan. So let's examine the triclosan.

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DR. SHE: We look at the triclosan. The experiment mass accuracy is 286.9439. And then we compare with the theoretical values.

--o0o--

DR. SHE: And then -- also, that's an isotope fingerprint for triclosan have three chlorines. They have

four major peaks from chlorine plus carbon peaks, so you can see the red mark on the most left-hand side of the data matched, but they are very small peaks, and the major peak is matched. So we called 100 percent match. Kind of the percent based on the reverse search criteria. So all of the theoretical peaks was found in the sample -- urine samples, so we think this is a good hit.

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DR. SHE: At the same time, we also found other chemicals were found out, and like BADGE and bisphenol A, bisphenol AF a few musk chemicals. The musk chemicals we have both have the nitrogen groups. So the hit that means we found it. We need further evaluation.

And also the database, we put in a positive ESI and a negative ESI, so we tried to cover different chemicals respond in different -- analytical technique differently. We try to cover all of them.

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DR. SHE: So this a few highlights for these studies. So with this new instrument set up, and incorporate it with other analytical forms, we're able to profile different samples. For example, one -- like the study we did with the UC Berkeley commercial pre-intervention, post-intervention, and we can see target compound different. We also can see the other untargeted

compound that may also have difference.

So ability to identify emerging chemicals or any chemicals is heading there. It's not new, but always there, but we can have a potential to identify them.

Another possibility, we can put all our analytical procedures together with one method and then do a high throughput screening. We didn't try that one yet, because this -- this new machine allows you to do multiple compounds. Again, can't do this with a co-dependent kind of analysis. You can do the post-analysis on the aliquoted data.

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DR. SHE: And we are -- I'll finish my talk with my planned future work. We are still working on the BPA analogues, and then we hope by next meeting we have completed. It's delayed for some technical reasons, but we are confident the next meeting we will finish it. And expand our current TCF database by collaborating with other groups, and then to see if we can get to -- share that database to put into our machines, analyze Expanded BEST samples, and continue automation of the sample preparation to enhance our laboratory analysis throughput.

Thank you.

ACTING CHAIRPERSON BRADMAN: We can take about two minutes if there's any clarifying questions right now,

or we can hold that off. Does anyone have any immediate questions.

PANEL MEMBER CRANOR: A really quick question about this. When you've compiled your -- I mean, I like the direction you're going, because I think the Biomonitoring Program has had obvious limits with respect to anticipatory issues. This is an anticipatory direction. Do you link your toxic substances database with toxicity then? I mean you've got this list of chemicals, what are the analogues? Where would you suspect that things are going to come up?

So an invented example. We had bisphenol A and then that's maybe being replaced by bisphenol S. And now is bisphenol J out there -- that's a new terms -- but is there a way to do that kind of anticipatory testing and getting clues to toxicity?

DR. SHE: I'm sorry. I need to make sure I understand the question. You think how we build this mass spectrometer database?

PANEL MEMBER CRANOR: I'm sorry?

DR. SHE: The database how will be the linkage between --

PANEL MEMBER CRANOR: Yes.

DR. SHE: -- our database and the toxicology database?

PANEL MEMBER CRANOR: Right. Right.

DR. SHE: Yeah. So far, we haven't planned to do that, but maybe an off-line database, because the machine generates the information direct link to the database that we are working on. So maybe on the off-line how to use the toxicology database help us to expand our database, that's what you're suggesting?

PANEL MEMBER CRANOR: The thought is this just seems to hold substantial potential, and I hope you keep going in that direction.

DR. SHE: Okay. Thank you.

ACTING CHAIRPERSON BRADMAN: Why don't we pause now and then, Dr. Petreas, we can hear your presentation, and there will be some more opportunity for questions on both presentations afterward.

(Thereupon an overhead presentation was presented as follows.)

DR. PETREAS: Okay. Thank you. Myrto Petreas. I will give you an update on the Environmental Chemistry Laboratory activities.

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DR. PETREAS: So basically, I'll give you an update on the progress we've made analyzing samples. And this has been really our major work over this time. We had a lot of deadlines and we have a lot of progress made.

Also, I will mention some other activities that we do for our department that directly or indirectly benefit this Program. And finally, I'll also add our status with the instrumentation again for identifying unknowns.

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DR. PETREAS: So we've been very busy analyzing samples for the various studies. And I'll start with the Three Generations, or 3G, Study that I have presented before. We had a deadline to meet, so all our efforts were made for this project.

This is a big study, a part of the Child Health and Development Program that Dr. Cohn has been funded from NIEHS, the National Cancer Institute, and the California Breast Cancer Research Program to undergo. It covers about 20,000 pregnancies that took place at Kaiser Oakland from the late fifties to late sixties.

And within this big universe, we have the Three Generations Study. And this looks at mothers, daughters, and granddaughters. That's why it's called the Three Generations. And I'll only mention the things that apply to us, our work for the Program.

We just completed analysis of maternal samples. These are perinatal samples. These women were pregnant in 1959 to '66. And the bulk of the work so far has involved

the mother's samples. In addition, their adult daughters had been contacted and 300 of them were sampled between 2011 and '12. And we also had these samples in our to-do list.

So basically, the maternal samples, as I said, were collected from '59 to '66. And if you look at the left-hand box, the median age was 26 years old of these mothers from 16 to 44. And their race was basically mostly white. The daughters now are already older. So the median age of the daughters now are 50 years old. And that study really targeted black daughters, black women. So half of them, if you look at their race breakdown, was the targeted group.

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DR. PETREAS: So we have basically completed all the samples. And we analyzed them for perfluorinated chemicals, PCBs, and organochlorine pesticides. This was both for the mothers and the daughters. And then PBDEs and hydroxy-BDEs were done only in the daughters, because we had shown years ago that these chemicals were not present in the mothers as expected. And, of course, everyone had their lipids done, so the results could be expressed on a lipid basis. So we're very happy to meet our deadlines and complete all this work.

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DR. PETREAS: And important for the Program is that, first of all, these results will soon be returned to the daughters by the principal investigator staff as part of a report back pilot study they're doing. So once the women receive the data and that part of the study is completed, then the aggregate results will be posted on the Biomonitoring California website.

So this is our plan to augment the Program, and -- you know, this agreement between the PI and us is very -- it helps the Program sustain itself, and that's the route we want to go in the future. So that was a 3G Study where most of our work was done.

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DR. PETREAS: The next study I want to mention again is the California Teachers Study with Reggy Reynolds as the PI. This also was funded by the California Breast Cancer Research Program. The recruitment and sample collection is still underway. We started in 2011, and we expect to complete it by the end of this year.

And so far, we have blood samples from about 1,000 breast cancer cases and 1,400 controls from the entire State. This is, of course, a breast cancer study, but has other secondary objectives that help our work here.

This is an older population of women, so it's

interesting demographics. I believe the median is around 65, but -- and the oldest one is 94. And the samples have been analyzed for PCBs, PBDEs, perfluorinated chemicals, thyroid hormones, and lipids.

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DR. PETREAS: And this is a chart I have shown before, and I'm highlighting in green when we have some progress. These chemical classes are analyzed separately. There are different silos that the samples go through. So we haven't much changed for the perfluorinated chemicals, because we had most of them done, but we made a lot of progress in the extraction and instrument analysis of PBDEs and PCBs and pesticides.

And we have released for the first time PCBs and pesticides to the principal investigator, and these will be posted on our website. And soon, we hope that we have more progress and completion, but we still haven't received all the samples. It's a very long and big study that will generate a lot of data for a very interesting demographic.

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DR. PETREAS: Our third study, which again is a collaboration with UC Berkeley. It's a childhood leukemia study, and that's also completed. This started -- we had done a lot of work on dust from homes of cases and

controls of children with leukemia and controls. And now we have blood from mothers and from children, these are the cases, whose dust we have already analyzed. Again, it's different objectives and different levels of complexity, but the important thing for us is that these mothers' blood samples were part of the Request for Information we had issued, and the investigators were the ones selected to work with us, and I'll return the data to them, and also the children. And publication will be coming soon from that.

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DR. PETREAS: So some other work that we're doing for our Department. This is a study that started a few years ago. Dr. Kim Hooper, who is now retired, was the principal investigator some time ago, but trying to finish it now. So in collaboration with the Santa Rosa Birth Center, we had collected -- contacted first-time mothers.

They were sampled between 2010 and 12. We have 65 of them, and we have pairs of serum, cord blood, and also breast milk. And we're completing the analysis for PBDEs, pesticides, PCBs, perfluorinated chemicals, and hydroxy-BDEs. We also have house dust from the homes, but we haven't started that. We also have exposure assessment questionnaires.

This is a study, which was partially funded by

U.S. EPA, and we're preparing some abstracts for upcoming conferences. And hopefully that in the next meeting we'll have some data to show to you, because this again can be part of our -- the aggregate data can also be shared with the Biomonitoring California website.

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DR. PETREAS: Good news. We got funded with -- along with UCSF, they're the principal investigators, to continue looking at PBDEs and hydroxy-BDEs in pregnant women from the San Francisco General Hospital. Recruitment is underway. The plan is to get 50 samples this year and 120 next year. And the very interesting thing is this is the same demographics with the previous studies we've done with them 2008 and '09, 2011-12. And on those two studies, we showed statistical significant decrease of PBDEs and hydroxy-BDEs in the serum of these pregnant women.

So it's very interesting to really determine the trends once we add these other data points here. This is funded by NIEHS, and Dr. Woodruff is the PI here again.

So that's for future. And again, Dr. Woodruff has agreed to release the aggregate results as they become available with our biomonitoring website. So again, we're building up more data than we could obtain on our own studies alone.

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DR. PETREAS: We also try to disseminate all this information and data. And since we met last time, we have three publications all by Dr. Whitehead. He's a post-doc that was part of his dissertation. So it's great to have energetic post-docs publishing quickly. So this has to do with all of the dust work that we have done on PAHs and nicotine and PCBs. And we have already mentioned the PBDEs, which was the first paper that came out. So these were recently published.

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DR. PETREAS: And we have quite a few manuscripts. And we talked about the comparison of the blood drawing tubes comparing the serum separator tubes with the traditional red top tubes for the POPs and PFCs and lipids. And this paper now is under review. We're actually responding to reviewer's comments.

Also, under review is the other analytical method to expedite and measure the polar compounds, the hydroxy-BDE's in human serum by LC-MS. And also submitted is another dust paper, looking at novel brominated flame retardant dust.

We also have manuscripts in preparation. And from the FOX study, our firefighters exposure to POPs is almost ready to go. We also have another dust paper

comparing the chemicals, PAHs, and POPs in fire house dust as opposed to residential dust.

And also, we're working on another methodological paper to look at BPA, bromophenols, and TBBPA in blood. So we keep busy with that.

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DR. PETREAS: Finally, I mean, we talked about the instrumentation for identifying unknowns. And the idea was that there are so many chemicals out there that would be potentially of interest to the Program, so we need to identify.

So after long discussions, we selected the instruments. This is bought by CDC, and we had to comply with their criteria. Staff developed pretty complicated criteria lists, talked with vendors, talked with users. And finally, I guess the decision was to buy the Agilent iFunnel QTOF 6550. I don't have a photograph for that. We only submitted the PO. Shipment is underway, and we expect to install it by a couple of months.

So we're really very excited.

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DR. PETREAS: And I really want to thank all of us -- all of the people who helped us come to the selection. First of all, the CDC for funding advice. Our Program staff are reviewing, and evaluating, and setting

up objective criteria to come to the decision. Especially Dr. Fiehn and his staff really helped us with multiple visits and telephone conversations and trying to weigh options. The same thing with many other users with various different systems that share their information. This was like a dynamic industry. Obviously, the instrument vendors who tried everything to convince us that their instrument was the best, even though they knew only one would be selected, and we finally selected one.

Now, I won't say that we have formed the unknowns committee by Dr. Park from our lab, Dr. She, and Dr. Krowech from OEHHA, so we can coordinate. We already heard that our sister lab is already ahead of us, obviously. And we need to learn a lot from them and from each other. And having this group coordinate and prioritize would help us. And we're really, really excited with this opportunity for the future.

That's all I have to say.

ACTING CHAIRPERSON BRADMAN: Thank you, Dr. Petreas.

That's really great progress, and really interested in the new instrumentation you have. We have some time now for the Panel to ask clarifying questions both to Dr. Petreas and Dr. She on any of the topics raised during the previous presentations.

So, Dr. Cranor.

PANEL MEMBER CRANOR: Thank you. On the Three Generational study, there are a couple of different reasons you might have for doing the Three Generational. And you're looking at, as near as I can tell, pretty persistent substances.

Is the idea that maybe these substances were transgenerationally transmitted from mother to daughter to granddaughter or -- and that could be one thing, or you're just looking at exposure levels and how those have changed over time, and can you separate those out?

DR. PETREAS: I can summarize a few that I'm familiar with. This is a very big study. Yes, indeed, we want to see, first of all, transgenerational transfer, but also in utero exposure affecting disease outcomes. This is a breast cancer study done to see --

PANEL MEMBER CRANOR: Okay.

DR. PETREAS: -- the potential of breast cancer based on the maternal serum. And the third generation will be again different endpoints based on the grand maternal serum.

PANEL MEMBER CRANOR: Very good.

DR. PETREAS: It's a very complex, a very, very valuable resource and we're very happy to be coordinating with them and sharing some data here.

PANEL MEMBER CRANOR: Very good.

ACTING CHAIRPERSON BRADMAN: Any other questions or comments?

Dr. Fiehn.

PANEL MEMBER FIEHN: Oliver Fiehn. I'd like to know for both laboratories which kinds of software you have explored so far and what types of software you are planning to explore?

DR. SHE: There are many software there. We just installed, for example -- right now, we look for -- we use TraceFinder from Thermo, so that's -- because that's very close link to their hardware. And then a lot of software saves. Since our machine right now can only do accurate mass and isotope profile some MS/MS tree software, like we may not able to take advantage, because we don't have that kind of data.

So the other software from, for example, Scripps Group, I think are called XCMS, stand for Exact Mass, can be used. METLIN, I'm not sure we can use right now.

So we look for the public available softwares. And also, we are aware your group developed Binbase, the experience we can use possibly for the GC. And so the machine we use also have a feature, don't have MS/MS feature, but have a feature code AIF, all-ion fragmentation, which is an insourced fragmentation with

the high collation energy. And we are aware the UCSF Rose Group already started to build some database in that. We couldn't use it.

So this is a few of the examples, but we'd like to learn more which other ones may be relevant and we can use them.

DR. PETREAS: I don't have much to add. I would defer to the Committee anyway, but we're getting the Agilent software that comes with it. And from there, we can, of course, explore all of the other things that you know.

ACTING CHAIRPERSON BRADMAN: Do you want to follow up on that? Okay. And then after that, Dr. Quint has a question.

PANEL MEMBER FIEHN: A follow-up comment maybe. I find it very encouraging that you have found triclosan using this untargeted way, because you, of course, knew where to look, right?

It is very important for both of these groups to carefully validate approaches. Otherwise, you will drown in too many compounds and too many features and too many things to look for, in terms of true positives and true negatives and false negatives and false positives. So it's very important to validate your parameters in your software searches, so that you don't like get too many

things to look at.

Also, of course, I'm happy to continue to advise on -- and my group on future updates of software, including other types of software that you haven't mentioned yet. Also, in terms of stability of the high throughput operations that you mentioned, because you then come into the problem unlike in targeted assays, where you know where to look. And what your criteria are in untargeted, you will find it much more complicated, because of the many peaks that are present.

And additionally, of course, I would encourage using a lot of quality controls. And you haven't mentioned the blank controls, but I would presume you use blank controls a lot. So just make sure that you always have these blank controls that are, you know, carefully monitored there too, including your enzyme assays. I presume this was a deglucuronidation assay and you should specify I think what you've used.

DR. SHE: I think all of the points you mentioned very important, how to avoid false positive, evaluate putatively at least, and we still do not get to the criteria yet to avoid -- to get a too long list to become a mini list.

The quality control and the areas are definitely I think are the experience you have on presenting at the

last meeting were many of the good points. We need to get on. And then also the last point, I actually missed the last point.

PANEL MEMBER FIEHN: You said you used an enzyme kit before. I presume it's a deglucuronidation, so you know, you didn't specify what kind of kit you use.

DR. SHE: Actually, you are right, and deglucuronidized, yeah.

So for the software -- you also mentioned software. We'd really like to exchange experience with you and then see how we can benefit mostly from our Science Guidance Panel's experience.

DR. PETREAS: Yeah. I totally agree. And I just want to add again personally thank you very much for you and your staff. And we plan to send staff for the training you have in September. Hopefully, by then we'll be set up and we'll know where the on and off button is.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: Dr. Quint.

PANEL MEMBER QUINT: Julia Quint. I had a simpler question. In terms of the unknowns, usually when chemicals are substituted, you know, they stick very closely to the same structure activity relationship. So I was wondering, you know, I think the value of this is the emerging -- looking at emerging chemicals. And I'm just

always interested in whether or not we can get a step ahead of, you know, where the industries are going or whoever is substituting the chemicals, because the minute a chemical is targeted or listed, then there's an immediate search for something that isn't targeted or listed.

And I was wondering in your -- how these two things emerging in terms of your use of this instrument, whether or not you're looking at structure activity relationships of some of the chemicals that we've already -- that are targeted and seeing if you can -- you know, are able to pick up, you know --

DR. SHE: Actually, that's a very good thought, and we then we thought about that too. The reason is, for example, this MS, mass spectrometer detector, itself we call a universal detector. That sees all of the mass, so because replacement of the old chemical, for example, BPE, they may replace it with BPAF structure similarity or the substructure of the two chemicals may be identical.

So how to look this same group or same type of chemicals with technology we have, so we didn't mention that, for example. That means we needed to have a selective target detector, which is a lot of the high MS/MS unknown. It actually ends up fair -- I also work in the newborn screening.

I'll give an example. For example, we look for all of the 21 immunoassays to look for the newborn defect. All of this immunoassays have the common feature which lost the common neutral loss, the mass is a hundred zero two. So the mass spectrometer can also do this grouping by looking for the common species or common substructure. So that's, for example, for the immunoassay that you can look at common neutral loss to say, oh, they are same group, or for us you can look for the same ions. So that's other technology we are thinking to work on.

PANEL MEMBER QUINT: Good.

DR. PETREAS: If I can add, Dr. Quint.

ACTING CHAIRPERSON BRADMAN: I should mention, we are getting into our time for public comments, so if we could just keep this comment short or response short.

DR. PETREAS: I guess the BPA analogues is the easy one. But if you think of PBDEs replaced by Firemaster, we're going to talk totally different structures, you know, the phosphates. So it's not something you can anticipate. It's whatever the industry found to replace and give the properties they want to give.

PANEL MEMBER QUINT: And we're keeping up with some of that, and Gail is constantly coming up with new tox analogues that people are going to, so that's good.

ACTING CHAIRPERSON BRADMAN: Anymore brief questions?

I think I'm going to interrupt now to keep us on track. And we now have some time for public comment. We have one -- again, one person. Veena Singla again who would like to make a comment related to the laboratory update.

Thank you.

DR. SINGLA: Thank you. Veena Singla, Natural Resources Defense Council. And I had questions for Dr. She and Dr. Petreas.

The HERMOSA Study was really interesting. And I was wondering what the timeline was for completion of those results. The comparison wasn't presented in terms of before and after the product use with the low chemical. So it would be really interesting to see that comparison. I wondering what the timeline was for those results?

And my other question for him had to do with the TCF database. He mentioned a number of sources that the chemicals in that database were pulled from. And I wondered if there was any relationship to the long list of chemicals of concern for the Safer Consumer Products Program for that TCF database? Because that could provide really valuable information to input into the Safer Consumer Products Program process, if we could get more

information on those particular chemicals of concern.

And then my last question was for Dr. Petreas had to do with PBDE flame retardant replacements, which was just brought up. It was great to hear that Dr. Woodruff's study on PBDEs would be ongoing as those studies have already shown the success of policies to restrict PBDEs. And I wondered if there was any plans to look at other flame retardants as well, given the recent policy changes in California on flame retardants in furniture to be able to track any progress resulting from those policies.

DR. SHE: Actually, for the first question, may I refer to Dr. Asa Bradman to address the timeline.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: Sure. Just to say the HERMOSA program is actually funded by the Breast Cancer Research Program. And we successfully worked with a group of high school students in Salinas and collected the samples. So the results for the study right now are in data analysis and we're working with student participants to do that.

I think the more aggregate information will stay on the Biomonitoring website until we're farther along in returning results to participants. And actually, we're going to be writing a paper with the high school students. So it will probably be, you know, six months -- six to

eight months before that will be more generally public.

So I should say too -- I'm going to take a minute to -- I want to publicly thank the Biomonitoring Program and CDPH for hosting a field trip by the HERMOSA high school students that have been working with us in Salinas. For those kids -- all those kids come from families where no one has ever, you know, been to college or even gone much beyond and 8th grade education. So we really appreciated that -- hosting that field trip a couple of weeks ago, and it really opened some doors for them.

Thanks.

Dr. Cranor.

Well, I should interrupt. Did you want to add to Veena's question or --

PANEL MEMBER CRANOR: It's on the HERMOSA Study.

ACTING CHAIRPERSON BRADMAN: Okay.

PANEL MEMBER CRANOR: As I was looking at that, I had a sociological question. That is, do you regard the young women who were using these products as typical or are they likely to use more or fewer of these products? It seems to me there's a representative sample question here, and I was curious about it.

DR. SHE: Maybe again Dr. Asa Bradman.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: Okay. Just briefly.

Maybe we can talk about it a little bit more at lunch, but the study is definitely a convenience sample. However, there's relatively little data on especially Latina teenagers and the Latina population in general. And in general, that population relative to other groups, uses more of these products.

If you even go into NHANES and look at, on a nationwide basis, exposures to personal care product-related chemicals, we tend to find higher levels in women compared to men. So that's why we kind of zeroed in on this project, but I'd be happy to talk about that maybe offline.

So Dr. She.

DR. SHE: So the second question you have about safety chemicals?

DR. SINGLA: Safer Consumer Products chemicals of concern list.

DR. SHE: Yes. Definitely we like to work -- expand our current TCF library, and include some more chemicals you mentioned. The third question.

DR. PETREAS: Myrto Petreas. Very short answer, no.

(Laughter.)

DR. PETREAS: No. No other flame retardants are planned for that study. There are many other biological

assays, but no flame retardants.

ACTING CHAIRPERSON BRADMAN: I think that's the end then of our public comment period at this point. I don't know if Davis Baltz is listening, but we maybe miss you a little bit right now.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: And we now have some time for additional Panel discussion, if there's more questions related to the presentations or anything that's been talked about this morning.

DIRECTOR ALEXEEFF: George Alexeeff with OEHHA. So it seems there were a number of questions with regards to the new instrumentation that is -- or being obtained at DTSC that is at -- in DPH and that is also available at UC Davis, UCSF -- I'm not sure where else -- and that there was discussion of some collaborations. And there was also some discussion about different instrumentation set-ups. I don't know. I think that was referred to. I don't know if you caught it, but there's different -- whether you have a mass spec or not have a mass spec, and that kind of stuff, and the discussion of collaboration.

And so I was wondering if it would make sense sometime in the future to have more discussion about those issues, what sort of barriers there are to collaboration. I don't even know what the issues are with in terms of

sharing the data -- the information that you have in terms of the structure on the databases, how -- if that's just freely shared or there's some issues with regards to that?

And then also the question of validation. There was a discussion of many peaks. I forget who was -- I think Myrto was mentioning that. And then how one goes about validating what chemical that actually is of a slough of possibilities. So I don't know maybe that might help the Panel just understand more about this new -- I mean, I know we had a presentation before. But now I think we're getting into more details and there's going to be, I think, more issues. And for the Panel to help, that might be something to do in the future.

ACTING CHAIRPERSON BRADMAN: Dr. Cranor.

PANEL MEMBER CRANOR: Carl Cranor. I keep forgetting to say that.

Following up the comment here, I know that there have been studies of medical delivery, and instruments that assist in diagnosing disease and so forth like MRIs. And there was a time when everybody hospital needed an MRI. And that's a very inefficient use of big machines.

So just to kind of follow up your question, is there someway to have an efficient number of big machines that are sort of well calibrated, and lots of people use them? I mean, that might be -- I don't know who controls

that, but each institution may want their machine just as -- but, just as not every medical -- not every hospital maybe needs an MRI, you need a certain number to handle the burden in a local area. So just add to that question.

ACTING CHAIRPERSON BRADMAN: Dr. Fiehn.

PANEL MEMBER FIEHN: Since these are new areas, I, you know, definitely would encourage, you know, having -- or also recommend having this team of these, how do you call it, panel of unknowns or so coordinate it between the labs, and I'll be happy to participate or coordinate efforts in the work -- in a workshop maybe, you know, where we could discuss these tests on data sets, for example, in Davis, but also happy to do it in other locations.

And, yes, all the efforts in the public domain say, you know, MZmine, XCMS and so on, are always addressing data from different sources, so from different vendors. So all the software that I know that has been created in the public, always tries to steer away from vendor-specific solutions. And I think therefore it will be interesting to even have like maybe compare, you know, samples that are tested on one machine and on the other machine with one or the other type of MS operation, and also, you know, it was spiked in samples and so on.

So this is definitely something that is of

interest, not only to these two programs and to, you know, appropriate samples to them, but also for the general public -- scientific community public.

ACTING CHAIRPERSON BRADMAN: I just want to respond to that as well. I think your comment is important. And it also speaks to the need to establish laboratory centers and resources outside of CDC. And I think that the California Biomonitoring Program and the resources that have come from CDC in terms of technology transfer and equipment purchase has been a big step towards establishing this region as kind of an independent laboratory center from CDC. And the kind of collaboration you're talking about I think is extremely important, because as we know, the CDC analyses have been kind of limited in their ability to really address I think a lot of the exposure environmental health issues nationally.

And that I just want to underscore, I think, the importance of what you're getting at is what -- just how important what you're getting at is, that we really need to have an independent kind of laboratory consortium, and working system here that really supports environmental health research and public health needs of the State. Maybe be extended to, you know, west coast or that sort of thing, but I think California really is at the forefront on this, and really want to suggest that as a direction to

go in.

So if there's not anymore discussion or recommendations to be made -- I'm seeing silence on the Panel at this point -- then I want to say that we're going to be taking a break for lunch soon. Prior to that, we're going to have a comment from Fran Kammerer -- am I pronouncing that right? -- Staff Counsel for OEHHA to give us a reminder about the Bagley-Keene Open Meeting Act.

I want to reiterate what I said earlier. We're ending about on time, and we're going to resume promptly at 1:15 p.m. So you have just barely an hour for lunch. So we can't sit down and order too many things and have to wait and then get here late.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: So we're going to start promptly at 10:15, so -- at 1:15, so don't go for junk food/fast food, but try to go quickly for lunch. Thanks.

STAFF COUNSEL KAMMERER: Frank Kammerer. Just I'm sure you're all experts at this already, that Bagley-Keene requires you to not, shall we say, meet outside of the public forum. So if you could just refrain from discussing matters of the Committee during lunch, that would be great, and discusses them here in the public forum.

Do you have any questions on that or -- I mean, it's okay to meet two people or so. We're just avoiding a quorum. Is that okay?

All right. Thank you.

(Off record: 12:05 PM)

(Thereupon a lunch break was taken.)

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

(On record: 1:15 PM)

DIRECTOR ALEXEEFF: Well, it's 1:15. And as Dr. Bradman had said, we're going to reconvene at 1:15. So here we are. So I will call the session back to order.

ACTING CHAIRPERSON BRADMAN: Okay. I want to welcome everyone back from lunch, and the meeting has now been called to order. The next agenda items are going to -- agenda items include consideration of selected metals as potential designated and potential priority chemicals. And I want to introduce Sara Hoover, Chief of the Safer Alternatives Assessment and Biomonitoring Section of OEHHA, and later we'll hear from Dr. Ryszard Gajek from the Biochemistry Inorganic Group at CDPH. So we look forward to this afternoon's session which I think will be very interesting.

Thanks.

(Thereupon an overhead presentation was presented as follows.)

MS. HOOVER: Thank you for the introduction, Asa. And as Asa just said, we're going to be considering today with the SGP chromium as a potential designated chemical. And we'll also be looking for the Panel's input on 11 currently designated metals in terms of whether the Panel thinks they should be priority chemicals.

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MS. HOOVER: So I just want to give you an idea of the structure of the agenda item. First I'm going to give you a brief overview of the status of various metals under Biomonitoring California. Then Ryszard will outline the current Environmental Health Laboratory capability to measure metals. And I want to just note that that's actually one of the reasons we're bringing metals to you because of this method that EHL has developed, this flexible, inexpensive, and excellent method.

Then after Ryszard's presentation, we'll go into the discussion of chromium as a potential designated chemical. After I present my slides, then the Panel will discuss and offer any recommendations that you'd like to on chromium.

Once that discussion is complete, we'll turn to consideration of the 11 currently designated metals to be considered as potential priority metals. And then at the very end, I'm just going to show one slide and invite the Panel and public to give some input after the meeting today on possible future consideration of other metals.

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MS. HOOVER: Okay. So this slide shows the currently designated and priority metals. The priority metals are shown in red. A couple notes on this slide.

The asterisks indicate for beryllium and platinum that CDC is actually not going to be measuring those anymore, and this is based on three survey cycles of non-detects. But I did want to note that these metals will continue to be designated under Biomonitoring California just by virtue of their inclusion in the National Reports on Human Exposure to Environmental Contaminants.

I also want to just note that vanadium is designated also as part of the complex mixture of diesel exhaust. We'll be discussing vanadium further when the Panel considers possible biomarkers for diesel exhaust. We're tentatively planning a discussion on that for the November 2014 SGP meeting.

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MS. HOOVER: So this slide also just provides one interesting note about additional designated metals that will be on the list as of April 2014. The date -- this date comes from the date when CDC is hoping to release their new updated tables. They've added these to the National Biomonitoring Program, but they haven't officially released the results as yet.

And then just a note from CDC, a further note, that we've been in discussion with them. They're also considering adding chromium and nickel to the National Biomonitoring Program, but they haven't made any firm

plans in this regard as yet.

And now, I'm going to hand off to Ryszard who will talk about the analytical methods.

Ryszard.

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DR. GAJEK: Thank you very much. I'd like to personally thank -- personally thank Dr. Hoover for letting me give this small presentation today.

All right. Okay. The title of my presentation is, of course, ultra-trace metals in blood, urine, and plasma by ICP-MS. And maybe I will correct myself regarding the first question I had today before.

For FOX, BEST, we measured in blood lead, mercury, cadmium, and manganese, so four metals in both.

All right.

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DR. GAJEK: All right. So metals -- toxic metals and part essential metals in bodily fluid are well at the bottom of ultra trace level. Most of them are at or below one parts per billion, or one µg/L. And as we know, a concentration of suspended and dissolved solid matter in all bodily fluid is really high and we are measuring really low concentration in such heavy metals.

We developed a method to analyze all these metals. I mean, I would target which one we measure, but

we measure in all three matrices. So in this case, it is not only blood and urine, but also human plasma. And our method is very simple. It is simple dilution of any of those biological material, and we introduce it directly to ICP-MS. So we don't separate. We have all these pesky solids inside, ICP-MS. Somehow we have no problem with measuring it.

And two important things. First, we introduced -- we changed the way a sample is introduced to the ICP-MS. And I introduced the concept of artificial synthetic matrices added to calibration standards, and altogether, resulted in very low method detection limits, and -- well -- and we started to use this method until we measured already a quite few.

And surprise, surprise, we started to -- detecting such low concentrations. And in case like a few metals like chromium and manganese, we find that before we didn't notice whether our lab was contaminated. And suddenly, we have this very low method detection limit, and found that we have to clean or wash all our lab supplies before analysis.

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DR. GAJEK: So in the second column -- in the second column, urine, EHL, it is our detection limit, and the panel of metals we measured. It partially overlapped

what CDC is measuring. And you can see that, if you compare these results, our method detection limits are quite lower than theirs. So we are quite proud of it.

All right. Okay. So anyway, what we can measure? A basic principle of mass spectrometry, anything introduced to plasma becomes ionized -- positive ionized, single charge ionized. And as such, we can measure any element we introduce. The matter is only what -- the concentration and ionization. So in short, generated signal intensities of signal generated, if the instrument is capable of detecting it. It is only regarding -- and we have so-called polyatomic interference.

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DR. GAJEK: In this example, we see a very common atoms or elements present in every biological fluid. Look at the first line has the same atomic mass like chromium, and, as such, would be detected as chromium. And this for first three decades of mass spectrometry was the biggest problem. At the end of last century, Perkin-Elmer introduced -- actually, they -- it was dynamic reaction cell, and later the other manufacturers follow the suit.

And we use helium collision cell, which is very effective in removing these polyatomic interferences, but it is always a price to pay. We also remove some useful signal and that way we have to compromise what we have to

remove or whatnot, and -- well, it is always a solution.

And the newest generation of ICP-MS supposed to be ten times more sensitive than the latest 7700. And these results in previous table were generated with first generation of ICP-MS made by Agilent. So potentially, this new instrument would be 30 times more sensitive, so imagine what we can do.

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DR. GAJEK: I have to hurry. Anyway, metal detection limit for all our panel is, as you see, this indication of our precision, and it is very good. And also, next, I highlighted a coefficient of variation, which is single digits, and means that -- and these data were generated over a period of two months. So day-to-day operation, of course CV, if it is equal to zero, it means that all measurements were exactly the same. So we are very close to it.

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DR. GAJEK: Okay. So keep point. Of course, this method is -- well, we judge by what -- a comparison of CV literature is very good, and it is very simple. It is very quick. We measure for instance in urine 12 metals, plus three internal standards, in two minutes, about two minutes. So, of course, it is very quick, rapid, and as you notice, it is also precise and accurate.

But with new instrument, of course, we could even improve our performance.

So this is already what I said.

And now, what we can measure. According to what I said before, that all positive ions, if we have enough signal, can be measured, actually there is no limit. And even more, non-metals and metals can be mixed, so we can design panel in which, for instance, would be iodine included or bromide, if we desire, so -- so in one shot, we can do everything.

And last note, any concentration above one parts per billion we can measure relatively easy, and -- well, there is a lot in this category. So if new metals -- and Sara will introduce the new possible panel members -- metal panel members would -- their concentration in bodily fluids are quite high, so we don't expect any potential problems.

All right. So thank you.

ACTING CHAIRPERSON BRADMAN: Thank you, Dr. Gajek. We have about two minutes for any clarifying questions. So very brief.

I think to stay on track then, then we'll continue with the presentation on chromium.

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MS. HOOVER: Okay. Thank you so much, Ryszard.

That was -- it's really -- that's again one of the main reasons we brought this item to you is because of the capability that EHL has developed on metals.

Okay. So now we're going to turn to consideration of chromium as a potential designated chemical. You received a document, and it's also been posted online, that summarized information relevant to the criteria for designated chemicals under Biomonitoring California. I'm just going to briefly outline that here.

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MS. HOOVER: So first just to clarify what we're talking about here. Chromium would be the entry on the list of designated chemicals. This would cover all forms of chromium and chromium compounds. Just a reminder, trivalent chromium is considered an essential nutrient, and hexavalent chromium is the toxic form. The hexavalent chromium compounds are listed under Proposition 65 as known to the State to cause cancer and reproductive toxicity.

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MS. HOOVER: So why are we looking at chromium?

In addition to the lab capability I just mentioned, chromium was suggested in the 2008 chemical selection surveys of State scientists and the public. Hexavalent chromium compounds are listed under Proposition

65. And currently, there are no data from CDC's national Biomonitoring Program.

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MS. HOOVER: This is just a reminder on the criteria for a designated chemical for Biomonitoring California, exposure or potential exposure, known or suspected health effects, the need to assess efficacy of public health actions to reduce exposure to a chemical, the availability of a biomonitoring analytical method, the availability of adequate biospecimen samples, and the incremental analytical cost.

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MS. HOOVER: So just a little bit about use of chromium in the U.S. It's used in stainless steel and other metal alloys. It's also used as a corrosion inhibitor and in protective coatings like chrome plating. Some of the other applications include as pigments and in catalysts, and it's a high volume in the U.S.

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MS. HOOVER: So now some notes on exposure. First, I'm going to talk about some information on potential exposures to hexavalent chromium in air.

Some possible sources, for example, chrome plating facilities release hexavalent chromium to air. This was formerly a major source to air in California.

The Air Resources Board and the State has focused on reducing these releases, and I provided some information in your document on that.

Welding also can release hexavalent chromium to air. Steel dust, for example in subways, is a possible source. Also, in cigarette smoke, and I found a recent report that it was measured in e-cigarette emissions as well.

So a little bit about air concentrations. The ambient air level is low. The State ambient air level is now low. Interesting though that it can be orders of magnitude higher in indoor air, if there's smoking present; similarly, in workplaces, such as metal fabricating, metal coating facilities, some construction sites, welding -- if something involves welding in the workplace, you can get substantially higher concentrations.

So just to put these numbers in context. Based on the unit risk level that OEHHA developed, the air concentration associated with a one in 10 to the sixth lifetime cancer risk is also very low. It's, in fact, even lower than the State ambient air level.

The non-cancer inhalation reference exposure level is 0.2 $\mu g/m^3$. And just a little interesting context, the OSHA PEL is 5 $\mu g/m^3$. So still substantially

higher. This PEL for hexavalent chromium was lowered actually in 2006 from 52 µg/m³ to 5.

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MS. HOOVER: Now, let's turn to chromium VI, hexavalent chromium in water. So the California Department of Public Health has identified two main sources in water in the State. One is industrial releases, both historical and some current, for example, from chrome plating facilities. It also occurs naturally in groundwater in some areas in California.

Here's a little bit on water concentration. So groundwater -- actually, the paper that I cited in the document was naturally occurring -- levels of chromium higher than 50 µg/L has been detected in aquifers in the western Mojave Desert in Southern California.

There was also monitoring of hexavalent chromium, and CDPH summarized the results from that monitoring, which was also in your document. Just briefly, from 2000 to 2012 hexavalent chromium was detected above 1 µg/L in about one-third of 7,000 drinking water sources.

So again, a little bit of context for you. The OEHHA public health goal for hexavalent chromium is 0.02 µg/L. This PHG was derived based on cancer risks for oral exposure to hexavalent chromium, and CDPH has proposed a maximum contaminant level for regulating hexavalent

chromium in drinking water in the State of 10 µg/L.

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MS. HOOVER: Okay. Another possible exposure, which is potentially of interest. So stainless steel and cobalt chromium alloys can release chromium, and Cr(VI) has been noted as the predominant species that comes off. So there's actually quite an extensive body of literature on elevated levels of hexavalent chromium in biological samples from patients who have had metal implants, for example knee and hip replacements.

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MS. HOOVER: With regard to the ability to biomonitor. So as probably many of you know, Cr(VI) is largely reduced to Cr(III) in the body, so speciation is not useful. However, it's been noted that actually measurements in blood and urine can detect elevated exposures to hexavalent chromium. The important caveat on that is that you need additional information. So if you see an elevated level of chromium in a biological sample, you need to couple that with some other information.

For example, if you're monitoring in a workplace with a known source of hexavalent chromium, if you have an exposure questionnaire, where you can evaluate what could this be coming from, what type of chromium? And then if you find an elevated level, you need to do some kind of

follow up most likely do a little quick survey to evaluate possible sources to figure out what's going on.

And I talked a little bit more about the complications of that in the document, so you can refer to that.

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MS. HOOVER: That being said, there's been a lot of interesting biomonitoring work done. And this is just a little sample to give you an idea. So there actually was a CDC trace element study that found 0.22 µg/L in the U.S. general population. In Europe, there have been several studies of the general population, all of them finding about 0.2 µg/L.

There was a study in New Jersey, and it turned out that resident children near a -- near chromium waste sites actually had elevated levels compared to controls in the urine. And there's been many, many studies on patients with metal implants. This is just one that I'm giving you as an example.

This was a study -- actually an analysis of studies in Europe, about 43 studies, 16 different implants, and these were hip implants. And they found a range in the studies, a mean range, between 1.3 and 2.2 µg/L in blood.

There was a study in Taiwan looking at resident

adults in a high density area of electroplating facilities versus elsewhere. They were able to detect an elevated level in these resident adults. Here's just an example of welders in Germany after the shift. They found an elevated level in all welders and then a more elevated level if it was specifically stainless steel with greater than five percent chromium.

And then just last, another workplace example of chrome plating workers that had elevated levels in blood. The control workers also had elevated levels. Both of these -- both the workers and the controls had fairly substantial smoking habits, so that might be one explanation for that higher control level.

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MS. HOOVER: In terms of analytical considerations, you just heard pretty much everything you needed to hear about that. EHL can already measure chromium in urine. It can easily be added to the blood metals panel at a minor incremental analytical cost. And there's plenty of specimen sample available.

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MS. HOOVER: With regard to the need to assess the efficacy of public health actions, as I mentioned, it's not currently included in the in the National Biomonitoring Program. We didn't locate specific data on

chromium biomonitoring in California. So biomonitoring coupled with other information could help map exposures to chromium -- hexavalent chromium across the State.

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MS. HOOVER: So finally, what are the options for the Panel?

So just like usual, the Panel can decide to recommend chromium as a designated chemical for Biomonitoring California, the Panel could choose to postpone consideration, or the Panel could choose to recommend against designating chromium.

And with that, I'm going to turn it back over to Asa.

ACTING CHAIRPERSON BRADMAN: So, at this point now, we have five minutes for clarifying questions from the Panel for Sara Hoover and anything else we've listened to so far related to chromium.

Dr. Quintana.

PANEL MEMBER QUINTANA: Hi. Jenny Quintana. Why wasn't the CDC measuring it? Was it for technical reasons?

MS. HOOVER: You know, I'm not going to comment on that. I didn't specifically ask them that question. They're planning to -- they're likely planning to include it. As I mentioned, they actually did measure it back in

'98 as part of a trace element study. Yeah, that's all I'm going to say.

ACTING CHAIRPERSON BRADMAN: Dr. Quint.

PANEL MEMBER QUINT: Julia Quint. Did you mention the reproductive developmental effects?

MS. HOOVER: Yeah. All I mentioned was that it's listed as known to the State to cause cancer and reproductive toxicity. And it's also all endpoints, development, male and female reproductive.

ACTING CHAIRPERSON BRADMAN: Dr. Fiehn.

PANEL MEMBER FIEHN: Can you elaborate more on the toxicity effects? I mean, usually we get informed more about toxicity effects. And, you know, since it's all seemingly reduced to chromium III, you know, I'm not quite clear here.

MS. HOOVER: So I'm not going to go into the whole complicated pharmacokinetics of chromium, but it's definitely a concern. Hexavalent chromium is known to the State to cause cancer, reproductive toxicity, developmental toxicity. So the -- just the fact that it's reduced, at some point, in the body, that process of reduction actually is associated with some toxic effects. Now, I don't know if any other OEHHA toxicologist wants to comment further on this, but, you know, it's -- hexavalent chromium -- the reduction to Cr(III) doesn't negate the

toxicity of hexavalent chromium in the body.

DR. SANDY: Martha Sandy. So in studies where they've administered hexavalent chromium, they have shown these effects that Sara has mentioned, cancer, reproductive, and developmental toxicity. And they have also, through other studies on pharmacokinetics, shown that hexavalent chromium is taken up in the body, absorbed, and so the effect is attributed to hexavalent chromium.

ACTING CHAIRPERSON BRADMAN: Dr. Quint.

PANEL MEMBER QUINT: Julia Quint. I just wanted to mention too that Sara mentioned the PEL that is OSHA has adopted fairly recently of 5 $\mu g/m^3$, but the cancer risk to the workers at that level is 10 to 46 per 1,000 over lifetime cancer risks. So while they've adopted a new PEL, I just want to mention that the risk of cancer to workers is extremely high. It was higher before, you can imagine, because it was 52, but this isn't unusual in terms of OSHA PELs, but still quite a cancer risk.

DR. ZEISE: Just to add on the reproductive side --

ACTING CHAIRPERSON BRADMAN: Could you identify yourself?

DR. ZEISE: Lauren Zeise with OEHHA -- that the data came from studies in workers for the male

reproductive effects, basically welders, who were exposed. So the evidence base in humans was fairly large.

ACTING CHAIRPERSON BRADMAN: And another question isn't chromium VI associated with the groundwater contamination in the Mojave Desert?

MS. HOOVER: Yeah, that's what I commented on. Actually, that's not -- well, the thing I particularly commented on was naturally occurring.

ACTING CHAIRPERSON BRADMAN: Right.

MS. HOOVER: However, DPH talks about that industrial releases have contaminated ground water in the State, and I actually was in touch with Elaine Khan, who worked on the PHG for OEHHA, and even recently, you know, there was issues about releases to groundwater from like chrome plating facilities. So this is still an issue within the State.

ACTING CHAIRPERSON BRADMAN: Okay. Right.

Dr. Cranor.

PANEL MEMBER CRANOR: This is not exactly a clarificatory question, but I've believe we had -- also had blowing chromium VI near the Ontario Airport in the Riverside Ontario area. They had some piles of cement -- from cement plants, and it was blowing out over the neighborhood, so it was airborne as well.

ACTING CHAIRPERSON BRADMAN: So if we're done

with the clarifying questions, at this point, we have some time now for public comment related to this agenda item. It looks like we have two requests.

So the first commenter is Nancy Buermeyer -- I'm sorry. I'm forgetting how to pronounce your last name, apologies -- from the Breast Cancer Fund.

MS. BUERMEYER: Thank you.

ACTING CHAIRPERSON BRADMAN: And I should say there's two commenters at this point, so we have about five minutes.

MS. BUERMEYER: Well, I will take nowhere near that time.

ACTING CHAIRPERSON BRADMAN: Thank you.

MS. BUERMEYER: I am Nancy Buermeyer with the Breast Cancer Fund. And I wanted to speak in favor of recommending that chromium be a designated chemical. All of the -- many of the chemicals that are of concern are for breast cancer. And while the data is definitely strongest on cadmium, there have been studies that have shown higher levels of chromium in cancerous breast biopsies as compared to non- -- the biopsies of women without breast cancer. So there is a concern there.

And we've also seen it have estrogenic effect on breast cancer cells. So it is an endocrine disruptor. It is of concern for breast cancer. And I would encourage

the Panel to include this. And if I were channeling Erin Brockovich, I would also say please include this in what you're doing. Thank you.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: And our second comment is Veena Singla again from NRDC.

DR. SINGLA: Hi. Thank you. Veena Singla Natural Resources Defense Council. I just had a clarifying question if maybe you could speak a little bit more to how -- what the chromium that EHL can measure, how that's reflective of trivalent versus hexavalent chromium?

MS. HOOVER: So I'm going to speak for Ryszard here, but you -- I mean, it's total chromium. So that's why I'm saying in this case, it's -- speciation is not useful, but that was why I was trying to show examples of studies where you can see elevated levels. And this has been shown in many, many workplace studies and in controlled experimental studies.

So the issue is not -- you know, yes, you're measuring total chromium, but you have to couple it with the other information, and then you can make a judgment about what you're seeing in the samples.

Ryszard, did you want to add anything else to that?

DR. GAJEK: One comment. Before collision cells

were introduced, there are considerable difficulties with measuring chromium because of these polyatomic interferences. So I would consider all data before that really questionable. So, no, it is -- it was quite difficult analytical work to determine chromium. It was by catching chromium on a column, and eluting. And so very complex measurement. Now, it is very simple. It is -- we can actually measure it in a fraction of a minute.

So we have a huge opportunity to actually touch this subject now in a real way. I mean, we can measure many samples, so -- of course, and very accurately and precisely. So this is advantage.

ACTING CHAIRPERSON BRADMAN: So I think that then completes our public comment period. And now we have several minutes actually for the Panel to continue some discussions. And I know I have another question for staff, if that's okay. It's a little bit out of order here, but I think we're doing okay for time.

How would -- or maybe this is a discussion for the group as well. How would chromium biomonitoring data be used? For example, if we were to generate distributions of concentrations in biological matrices for the population, given that it's also an essential nutrient and we're getting total chromium, does it really tell us

anything about exposure to hexavalent chromium or would we have to have some sort of cutoff where there was follow up and maybe some questionnaires? And how would -- it seems to me there's a lot of complexity here with respect to how to interpret but also how to return results.

MS. HOOVER: Yeah. So the way that I see it, like I said, you have to use other information. I mean, that's clear, but we have a -- we have protocols already in place for that for other metals. And so we would develop a protocol just like that for chromium, so we can look at, you know, what cutoff would we use, what would we consider elevated, we'd write a follow-up survey, we'd have a protocol for follow-up testing, if needed.

So I -- yes, it's a challenge, yes, there are complexities, but I'm really confident we're up to that challenge and I think it's well worth it just to even look across the State, and start to map exposures. But we have a good process for putting things into context, explaining -- like manganese was another example. We did measure manganese in some pilot studies, and we had to do the same thing there. We had to explain essential nutrient. Above a certain level, you're going to have concerns. What is the approximate normal range? And we did all that, and it was successful those -- that result return effort. So I'm confident we could do the same

thing for chromium.

ACTING CHAIRPERSON BRADMAN: One question I have related to this is can you have chromium in the normal range, but excess exposure to chromium(VI)? For example, if you went to Hinkley or -- you know, there's clearly some examples here where there's over exposed populations, and you can see higher exposures that were probably due to hexavalent chromium, but are there going to be people that are going to get missed essentially where they have normal chromium levels that you might attribute to normal diet and nutrition, but they have overexposure to chromium(VI)?

MS. HOOVER: I mean, you know, again, I haven't researched that at this point, but that's something we could look at. I don't know if anybody else wants to comment? George, did you want to make a comment on that?

DIRECTOR ALEXEEFF: George Alexeeff. Just, you know, there's been a number of studies, animal studies, human studies. Trivalent chromium is very poorly absorbed. So you're not going to have a very high level. That's why, in terms of if you have elevations, it would pretty much have to be done -- due to hexavalent chromium exposure, because -- unless someone is somehow consuming very large quantities of trivalent chromium.

But I think even then, the absorption is actually very low, so -- in contrast, hexavalent chromium is

actually absorbed very well, so -- and that's one of the questions about well certainly by inhalation. Inhalation is a very important route of exposure, occupationally as well as Dr. Cranor was mentioning from cement, cement plants, cement piles. So those would be exposures that one could receive.

The question has been in terms of the reduction has mostly been from ingestion -- the ingestion issue. But even under those circumstances, there's a little bit of debate with regards to that, but the studies have shown, you know, at least the studies that have been conducted is that again it's not all reduced. There's a certain amount that's absorbed. It does result in an elevation. It does result in -- okay, if you were to consume trivalent chromium, you probably would not detect it or you'd detect very, very little in the urine. In contrast, you would detect -- it would be very detectable in the urine for hexavalent chromium exposure. Even if it's converted in the body to trivalent, you would not have received that dose, unless it was hexavalent initially.

Sorry I was so long.

ACTING CHAIRPERSON BRADMAN: That's okay. Thank you for that clarification. I think that was helpful for everybody in the room.

And so now we have time for Panel discussion.

Dr. Quintana.

PANEL MEMBER QUINTANA: Hi. I just was reading in your document, Sara, about the utility of red blood cell chromium. And I'm just wondering if you had thought about that as a follow-up test, if they came up high? In the total chromium, if you were -- thought that had any utility to explore that as perhaps proving it was hexavalent chromium?

MS. HOOVER: So I'm going to let Ryszard comment on red blood cells, but I did note some of the -- it's not a -- it's not a slam dunk, and I noted some of the difficulties in interpreting that.

PANEL MEMBER QUINTANA: Follow up.

MS. HOOVER: Yeah. So I'm going to -- Ryszard, you want to --

DR. GAJEK: As far as I know, chromium(VI), when it enters blood stream is immediately caught by red blood cells. It permanently binds until red cell dies. It is in about 56 days, so -- and we can measure separately in plasma, whole blood, and red blood cells. So we can actually, let's say, have a better picture of what happened, but Cr(III) apparently is not existing for long if it enters the cell.

MS. HOOVER: So I guess my answer is, yeah, we

could consider that. We could -- you know, I mean, I think that part of this will -- one of the things we always say is, you know, the chemical's designated and the Program determines the best way to measure it, and we have a lot of options with EHL to explore those sorts of things. So, yeah, we could explore that.

ACTING CHAIRPERSON BRADMAN: Dr. Fiehn.

PANEL MEMBER FIEHN: Okay. I'd like to give a second consideration to the statements that it doesn't make sense to measure or distinguish chromium(III) to chromium(VI). So since toxicity is different, and it's known to be different, and it's known to have different roots and to be important in biotransformations in different organs or in the red blood cells versus just direct secretion, it obviously makes sense to be able to distinguish both.

Now, that it's not possible, that's a totally different animal, right? I mean, it's a total different problem that we cannot easily distinguish. But would it be great if we could distinguish? Absolutely, because there might be people who would have genetic dispositions or other ways to, you know, to incorporate or maybe by different types of gut microbiota, different types of absorption.

So if we could measure them, it would be great.

Now, we can't, that -- you know, that's all right, but just to make -- to say or to state it doesn't need to be. It doesn't -- it's not important, that is not scientifically, from all I heard, valid. You know, so instead I would say it would be great if we could distinguish them. That doesn't mean we should not designate them. I mean, I want to make that clear. It just means that we should not stop with trying to improve methods, if we can.

ACTING CHAIRPERSON BRADMAN: Is there any other discussion or comments from the Panel?

Just to --

MS. HOOVER: Let me just pipe in. I just want to clarify, we didn't say that it's not important. It's just that given what is possible right now, this is how we're going to approach it. But, yeah, did you have any comment on speciation?

DR. GAJEK: It is very difficult to differentiate, because chromium(III) and chromium(VI) can coexist and can change valency very easily from one to another. It depends on pH, on composition, on many factors. So in how -- we measure both species in drinking water. At the moment of sampling, we have to add enriched chromium(VI) and chromium(III) separate isotopes. And then when we come to lab, we do isotope measurements. And

after very long calculation, we can determine what was at the moment on sampling, because when the water was transported from the sampling place to lab, you already changed valence. So it is very difficult.

ACTING CHAIRPERSON BRADMAN: So if there's no more discussion about -- Sara, did you want to say something?

MS. HOOVER: (Shakes head.)

ACTING CHAIRPERSON BRADMAN: No more discussion about what's been presented so far, our next task is to consider whether we want to designate chromium as a chemical for the California Environmental Contaminant Biomonitoring Program. And just to review criteria for designated chemicals -- now I'm going to opine on this a little bit -- I think the criteria include exposure or potential exposure. I think we see opportunities for that in California on a number of fronts.

I'm particularly interested in the joint part of it, when we think of and aging population and more of these materials being used, but also other environmental sources. Known or suspected health effects, I think that's pretty clear from the -- just given the fact that it's known to the State of California to be a toxicant in a number of different classes.

And need to assess efficacy of public health

actions. Clearly, there's a potential for follow up and intervention. Availability of biomonitoring analytical methods, we've had some impressive descriptions of new methods to detect at very low levels.

Adequacy of biospecimen samples.

I think when we look at these criteria on a number of fronts, chromium meets the bar for being considered a designated chemical. I don't know if anyone wants to comment on that or we want to move ahead with a vote on that?

Dr. Cranor.

PANEL MEMBER CRANOR: I have just a quick question. Those could be joint criteria that have to be satisfied or they could be disjunctive criteria. I took them to be more or less disjunctive, that you didn't need them all, but you needed one on more of them.

Sara, can you help there?

MS. HOOVER: You're right.

PANEL MEMBER CRANOR: Okay.

MS. HOOVER: Yeah, they're not joined by "ands", but nonetheless, we like to, you know, evaluate all of them.

PANEL MEMBER CRANOR: Right, as many as possible.

ACTING CHAIRPERSON CRANOR: Right. And I guess I would argue that -- or opine that chromium meets these

criteria at many different levels.

PANEL MEMBER CRANOR: Yes.

ACTING CHAIRPERSON BRADMAN: Any other comments?

Does anyone want to, or I will, make a motion? How about I'll make a motion? So I, Dr. Bradman, want to kind of submit the motion to the Panel that chromium be included as a designated chemical in the California Environmental Contaminant Biomonitoring Program.

PANEL MEMBER CRANOR: I, Carl Cranor, second it.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: Thank you.

Shall we have a vote?

(Laughter.)

PANEL MEMBER KAVANAUGH-LYNCH: Aye.

PANEL MEMBER FIEHN: Aye.

PANEL MEMBER QUINT: Aye.

ACTING CHAIRPERSON BRADMAN: Aye.

PANEL MEMBER QUINTANA: Aye.

PANEL MEMBER CRANOR: Aye.

ACTING CHAIRPERSON BRADMAN: Okay. So the Panel has made a unanimous recommendation that chromium be considered a designated chemical for the California Environmental Contaminant Biomonitoring Program.

My next question is do we want to consider this as a priority chemical or should we go on with the rest of

the presentation?

MS. HOOVER: That will be the last slide in the talk.

--o0o--

MS. HOOVER: Okay. So thank you for that good discussion, and on to the next topic.

Now, we're going to look at potential priority chemicals: selected metals.

--o0o--

MS. HOOVER: So a reminder about the criteria for a priority chemical. The degree of potential exposure. The likelihood of a chemical being a carcinogen or a toxicant. This can be on peer reviewed health data. It can also be on chemical structure or toxicology of related compounds. The limits of laboratory detection, including the ability to detect the chemical at low enough levels that could be expected in the general population, and other criteria that the Panel may agree to.

--o0o--

MS. HOOVER: Okay. So a little background for you. Back in 2009, many of you were on the Panel. And, at that time, the Panel looked through the designated metals and chose four as priority chemicals, arsenic, cadmium, lead, and mercury.

As we've heard, EHL now has the capability to

measure additional metals and has the flexibility to swap metals in and out of panels. So basically, your charge today is for you, the Panel, to give us input on which if any additional metals should be considered priority chemicals for measurement in California.

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MS. HOOVER: Under consideration today are these metals, antimony, barium, beryllium, cesium, cobalt, manganese, molybdenum, platinum, thallium, tungsten, and uranium.

--o0o--

MS. HOOVER: So as I -- you know, we had sent these materials to the Panel, and I noted that it essentially was just background information for you to have your discussion and make your recommendations. The summary information included notes on EHL capability, their current capability - but I'll note again what Ryszard said, he can pretty much measure any metal you ask him to - and the CDC status of these metals. There's also some information on use. There's examples of potential exposures. There's indications of toxicity based on secondary sources and some selected literature reports.

And I want to emphasize that again this table was just sort of a -- for your information, and it's not claiming to be a comprehensive summary of 11 metals. As

you can imagine, there's vast amounts of literature on these metals.

In addition to the materials that we prepared, we also sent you excerpts from CDC reports and from USGS -- a USGS report and extensive reference list.

--o0o--

MS. HOOVER: So basically, this is the Panel's opportunity to recommend one or more metals as priority chemicals, to postpone consideration of any of the metals, or to recommend no new priority chemicals.

ACTING CHAIRPERSON BRADMAN: So we now have time for basically the same pattern we've been having: time for clarifying questions and then public comment and then Panel discussion.

Dr. Cranor.

PANEL MEMBER CRANOR: Carl Cranor. On the criteria for priority chemicals, disjunctive or joint?

MS. HOOVER: As before, joined by -- not by "and".

PANEL MEMBER CRANOR: Not by "and".

MS. HOOVER: They're not joined by "and".

PANEL MEMBER CRANOR: I'm a philosopher. We distinguish between "or" and "and".

(Laughter.)

ACTING CHAIRPERSON BRADMAN: So anymore

clarifying questions?

This is quite a list. I know when I've been looking at this over the past few days, there's a lot to digest.

Dr. Quintana.

PANEL MEMBER QUINTANA: I just had a clarifying question about the method. I see the CDC dropped platinum, is that right, beryllium?

MS. HOOVER: Yeah, beryllium and platinum.

PANEL MEMBER QUINTANA: But is your method significantly more sensitive than theirs was, because they dropped it for reasons of non-detect, isn't that right?

MS. HOOVER: That's correct. I mean, I'm saying that's correct, that's why they dropped it. I'll let Ryszard comment on sensitivity.

DR. GAJEK: All right. Method of detection are quite flexible -- I mean, depending on what kind of instrument you use. This is the basic thing. We -- if we cannot detect, we can use additional methods, like enrichment, for instance, and always detect. It matters how much time and effort we want to spend detecting.

I believe, personal belief, if we have this new instrument, and with projected ten times better detectability, we can actually detect in one shot, which is, of course, a cost effective method.

So I would say it would be detected -- I mean, it would be able to detect. As an example, uranium, which is at a very low concentration, method detection limit for uranium is single digit, actually 1 ppt. And platinum is -- or beryllium is not any particularly different than any other metal. I am not sure how strong signal they gave under ICP-MS condition, but I believe one way or another we can measure it.

ACTING CHAIRPERSON BRADMAN: Dr. Quint.

PANEL MEMBER QUINT: Julia Quint. So am I to understand, so you have one sample and you can just measure all of these metals in that one sample. So we're not talking about extra -- a lot of extra time or a lot of extra sample?

DR. GAJEK: No. The panel is pretty flexible. We can actually add or include, exclude anything. It is practical matter not more than 15 so far. No more than 15 metals at once, because we have looped -- we fill loop with a sample solution, and as much of -- as long as we have solution in loop, we can measure, but after that, it is difficult.

So, I mean, in two injections, we can potentially measure 30 methods, right. And it is a matter of mathematics.

ACTING CHAIRPERSON BRADMAN: Dr. Fiehn.

PANEL MEMBER FIEHN: I have, I guess, a question for clarification. You said, you know, if you extend the improved capabilities, that means it's extended by your perception, but these are not validated methods yet. I mean, also, you know, in terms of you spoke before about lab contaminations about manganese I think it was. So, in principle, there might be other contaminations just, you know -- and also, you know, of course, you would need calibration curves for the different metal, so it's -- you make it sound very easy. I understand that we tend to like that, but is it really that easy?

(Laughter.)

DR. GAJEK: I like you to be skeptical, because it is very good question. And we struggle over time how we can measure our accomplishment, if it is good or bad or we fail? And how we usually do it, we have so-called standard reference materials, but we discovered when NIST, the most famous and most recognized material is failing many times. It is not accurate. And they have a reference value and a certified value.

And this reference value -- for instance, recently we finished development of serum metal, and they claim it should be like two ppb of mercury in it. And we find 0.2 consistently. Well -- and PT, proficiency testing, we receive usually samples which have

concentration that -- of those of dead people. I mean, mercury, this 80 parts per billion how can we detect 80 parts per billion of mercury in urine?

I mean, so we struggle all the time. But on the other hand, when we compare what we -- our method detection is with CDC we are much better, order of magnitude better. And this is -- these data are obtained with 12 years old design instrument. Imagine we can measure it now with the state of the art instrument, 30 times more sensitive.

So I am sure that -- you know, well, we have also second generation instruments, 7700. It is three times more sensitive than 7500. And we exactly observe like that more sensitive instruments we can detect, more method and easily, because metal detection limit is not only, let's say, devalued because it's a statistical value. We can detect it with 99 percent of certainty. But to have good value, I mean reliable valuable, it has to be involvement of detection limit.

Well, it is nice to have it five times to ten times above detection limit. And we pretty much have it for many metals, and -- well, of course, I can only promise, because I haven't measured, because nobody asked us, as a matter of fact, so -- because if somebody asked that, I would measure it.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: Okay. I think we're going to have a call now for public comments related to the potential priority metals.

Okay. We have one in-person public comment, and then we have a comment that was also submitted by email last night. So again, Veena Singla from the Natural Resources Defense Council.

DR. SINGLA: Thank you. I just wanted to speak in favor of including antimony, as it's widely -- antimony compounds are widely used in a number of consumer products, including textiles, upholstered furniture, and mattresses as flame retardants or flame retardant synergists. And I believe there's a number of antimony compounds already listed as known to the State of California to cause cancer reproductive or developmental toxicity. So I think it would be appropriate to include them for biomonitoring.

ACTING CHAIRPERSON BRADMAN: I'm going to just provide an overview. Sara, do you think it's a good time to comment on the manganese?

MS. HOOVER: Yeah.

ACTING CHAIRPERSON BRADMAN: Okay. We had a couple of comments submitted by email. And in particular was a letter from Joseph Green, who's Counsel to the

Manganese Interest Group, which I presume is a industry association.

And the letter is probably too long to read verbatim to the -- during today's meeting. This, of course, was posted online. It was received yesterday, and I'm just going to read a few of their points.

"On behalf of the Manganese Interest Group, we're pleased to provide the following comments regarding the potential listing of manganese as a priority chemical...". They also attach some comments that they provided to us, to the Panel in 2010.

They're particularly concerned about the designation of manganese as a chemical under the Program and interpreting the results. And here are some of the following points of particular significance.

"Manganese is a naturally occurring essential nutrient required to maintain human health. While an essential component of all bodily tissues, manganese accumulation is naturally regulated by the human body.

"Application of the human physiologically-based pharmacokinetic model shows that chronic exposure does not materially alter tissue concentrations outside the normal fluctuations that occur due to dietary -- due to changing dietary intakes.

"The PBPK model also suggests that blood and

urine are not likely to be good biomarkers of exposure...".

"As noted in previous comments...the Manganese Interest Group questions whether a biomonitoring program for manganese is likely to yield useful data.

"The background document prepared in support of the Scientific Guidance Panel meeting...", for today, "...fails to mention the critical findings of the aforementioned human PBPK model".

And with a little editorial insert by me, this model was discussed at our -- at that 2010 meeting, and I think we actually even had a workshop that included one of the developers of the model where a variety of -- it was an open meeting and Panel members were invited to attend.

"Further, the exposure data summary states that 'CARB reports a State average ambient air concentration of 17.8 ng/m^3 in 2012'. Such levels are well below even the most stringent estimates of safe levels of inhalation exposure for a lifetime".

And that standards -- a risk level proposed by the Agency for Toxic Substances and Disease Registry was set about 0.3 µg/m^3. So there's some order of magnitude differences -- several order of magnitude differences between this and also a reference concentration proposed by the Toxicology Excellence for Risk Assessment, TERA,

International Toxicity Estimates published a paper in 2011 proposing a manganese reference concentration of 2-7 µg/m³, so two to three orders of magnitude higher.

"The SGP background document also states that, 'Elevated manganese blood levels have been measured in welders'. While welders may be exposed to elevated manganese levels, this exposure scenario is not relevant to an assessment of manganese levels in the larger population. As the summary notes, '[m]ost manganese exposure occurs through diet.'"

And then there's some additional comments about detections of water -- detections of manganese in water throughout California. In some cases, there's been exceedances above health-based notification levels. But they argued that the -- they present information from the WHO that the health notification level is really too high compared to reevaluations by WHO about what is acceptable. That the health notification levels really are much too high relative to any risks.

And the, "MIG appreciates the opportunity to submit these comments and would be happy to provide additional information...".

So to kind of present a summary of this, and we should consider this as we go on with our discussions.

So I think that completes then the public comment

phase of this discussion with regards to priority metals.

And so now, I think we have kind of a difficult task before us to select which, if any, of these chemicals we should consider as priority chemicals.

I want to make a couple of points, since I have the seat right now.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: If I understand correctly, you're already measuring metals in many of these compounds -- I mean, in many of these materials. And, in fact, you're using the method, this method. So, for example, lead and other things that we've already prioritized are going to be measured. And essentially, by default, many of these metals are going to be measured anyway, is that correct?

DR. GAJEK: (Nods head.)

ACTING CHAIRPERSON BRADMAN: And I wanted to also ask for the lead measurements that come out of this method, are they essentially FDA approved and do they meet the standard for a blood lead test, at least when it's done in blood, in terms of being a certified medical test?

DR. GAJEK: Okay. First of all, we are a CLIA certified --

ACTING CHAIRPERSON BRADMAN: Yeah, certified, yeah. Excuse me.

DR. GAJEK: Oh, okay. We are also recognized by CAP, College of American Pathologists, and CDC, as a lab designated to analyze blood for cadmium, mercury, and lead. So we are checked.

ACTING CHAIRPERSON BRADMAN: And this particular method conforms to that certification?

DR. GAJEK: Yes, exactly. Exactly. We analyze and send the results of this.

And a comment on manganese. Manganese is one of -- difficult metals to measure, first of all, so called low mass analytes. They have a lot of interferences -- polyatomic interferences again. Before collision cell, it was very difficult to measure manganese. And even quite recently, a paper by a researcher from New York State Department of Health, their method detection limit for manganese in urine was 0.5 ppb, and ours is one order of magnitude lower, so -- and again, if we have more sensitive instrument, we can improve our measurements.

And we measure 20X diluted urine. We could go to 10X. It was not necessary. I mean, a frequency of detection at our metal -- with our method detection limit was good enough to detect, as far as I remember, 80 percent of manganese in urine. So we are pretty good in this department. We're fortunate.

And another comment. Recently, I listened to a

presentation of Dr. Wright from -- sorry, I forgot, but --

ACTING CHAIRPERSON BRADMAN: Bob Wright from Mount Sinai.

DR. GAJEK: Right, and his comment was that he actually measured manganese and lead in deciduous teeth using laser ablation, so he could point out 3 micron layer in polished tooth. And he found that actually it is kind of -- manganese is a co-factor -- or lead is a co-factor of manganese in some health effect. And they plan to extract DNA or RNA, any genetic material, from this layer and try to assess even better.

So my point is that last seven years basically, the results are reliable, more or less. We found the way to make it more reliable, much better. So we witness process when generated data would be much more accurate and precise. And if we can find correlations which never was -- were found before. So this is my personal belief.

MS. HOOVER: I just wanted to add one other point, which maybe the new Panel members might not know, which is these are all designated, which means we can measure them in any Program study right now, so the Program could choose to measure any of them. So by telling us what you think priority is, that would give -- you know, Ryszard guidance on should we swap metals in and out, are you interested in a particular metal? That's

really the purpose of your discussion here.

So they're already designated. We can already measure them. We could choose to expand the metals panels, but we really want your input on metals that you think are particularly important.

ACTING CHAIRPERSON BRADMAN: So I want to make some comments about manganese. But then I want to inform the Panel what I would like to do is go up and down the line and have each of us perhaps make some comments on metals that we would want to prioritize or not, so we can come up with a recommendation. So maybe while I'm opining on manganese, we can come up with some thoughts on this.

I appreciate the comments from the Manganese Interest Group. And I think there are a lot of challenges with biomonitoring for manganese and interpreting it in terms of health effects. It is an essential nutrient, and it's one of these strange substances perhaps a little bit like chromium versus chromium(VI), but with manganese -- overexposure to manganese it's very neurotoxic, and it seems to be that the inhalation route is probably most important where there can be travel to the brain through the olfactory bulb.

We've been looking at manganese in our work in the Salinas Valley, and manganese-containing pesticides are very heavily used in California. A few years ago when

we talked about this first, there was about two million pounds of manganese-containing fungicides used in California. Now, there's about a little over one million pounds, because one of them was deregistered, but they continue to be significantly used in California. In fact, agriculture is probably the biggest source of manganese compared to industrial sources in California.

We also see in our studies in the Salinas Valley that agricultural use and contamination in the home is associated with exposure. So there seems to be a fairly clear link between levels in teeth. We actually pioneered some of those laser ablation techniques looking at manganese in teeth. And we're able to look at pretty clearly prenatal and postnatal exposure to manganese, and environmental predictors of those concentrations.

With our data and also some other studies, we see some indication of possible health effects in children at a very young age. But so far in our group, when we look at early exposures and later development in the kids, we don't see any consistent health effects in terms of neurodevelopment. So that's, I think, an important piece to consider.

In contrast, the group at Harvard has been looking at manganese, both individually and in relation to lead exposure. And in several studies now, they've seen a

relationship between early exposures and neurodevelopment -- adverse neurodevelopment to outcomes in the children.

So their results are actually similar to ours at the young age, and they have not yet followed up at older ages, but there also seems to be a synergy with lead. And, in general, I think there's an argument that manganese is neurotoxic and it's likely that there could be concerns about environmental exposures.

So for those reasons as we go through the list, that's going to be one on mine that I think we want to consider as a priority while acknowledging the issues that the Manganese Interest Group brings up that it's hard to interpret what the biomarkers mean, but that's I think a challenge rather than an obstacle.

So shall we start, in terms of individual -- Dr. Cranor, have you --

PANEL MEMBER CRANOR: Well, I'm probably the least well-informed here. But looking at the criteria, and they're disjunctive, joined by an "or", all of them are toxic, many cause cancer. Manganese appears to be a neurotoxicant. I recognize there may be some detection problems. So I suppose my inclination -- presumptive inclination would be that unless there are reasons for keeping something off the list of the priority metals, I

would vote to list them all.

I would -- I'm willing to learn from the rest of you whether something should be left off the list, if it would overwhelm the lab or if something is obviously less toxic or clearly exposure is not a serious problem, things like that might matter. But it certainly satisfies the disjunctive criteria, it seems to me, all of them.

PANEL MEMBER QUINTANA: Well, I believe you did -- Penelope Quintana, by the way. I believe you did say you could do 15 at once. And by strange chance, if you add your other four, it adds up to 15.

(Laughter.)

DR. GAJEK: You know, I have to go a little bit deeper into methodology. Okay. So the time needed to measure anything in -- by our method is we simply fill a loop and we have time, physical time, how much time we can spend for detecting everything.

And it is -- each time -- I mean, for each metal we have to spend a set amount of time. So it could be fractional second, or three second and so on.

And we can -- with better instrument, the time is shorter. So potentially with new instrument, we could, with the same loop, measure 20 metals. It is actually almost certain.

MS. HOOVER: But I think, Ryszard, you also had

said that we actually could have -- we could have like a primary panel. We could have a secondary panel. I don't think measurement is an issue here. You know, I think actually -- I sort of like Carl's approach to it, which is, you know, you look at the criteria, you know, make an argument -- make an argument about either on or off, you know, what -- so Carl made his argument.

What we really want to hear -- I don't think the analytical is the limiting factor, so I would move on to, you know, the other criteria and your reasons for why you think it should be a priority for measurement in California.

PANEL MEMBER QUINTANA: I'd like to add to Asa, if I could.

ACTING CHAIRPERSON BRADMAN: Sure.

PANEL MEMBER QUINTANA: So before I came to this meeting, I was looking at the list trying to figure out why I would add something. And so the way I was doing it in my mind, I have interest in what other Panel members would think, but was -- if it had an occupational exposure, I automatically put it on there, because I think one of the most amazing things that the NHANES data that the CDC analyzed, when it first came out, was to give a reference level for what is around in people that aren't exposed. It helps people that work with the workers

interpret data.

And so I was thinking how very valuable that would be for anything with an occupational exposure, such as manganese, and molybdenum and other things, since I put those on the list.

And then I also put on the list anything that had a source of interest to Californians. And I put for smoking -- anything from smoking obviously I thought was important from tobacco smoke. Fracking, I think it was cesium. That, well, gee, if it's something to do with fracking, I would want to see that on there. And then platinum, even though it's non-detect by the CDC, if that was not an issue, it potentially at least could possibly show up as a marker of traffic, which is of great interest.

And so by the time I was done, I actually had them all on there.

(Laughter.)

PANEL MEMBER QUINTANA: And so I went from the bottom up and I ended up with the same list.

ACTING CHAIRPERSON BRADMAN: I guess it's my turn. I know my first set of priorities when I looked at this was to identify the ones that were listed on Prop 65, the Prop 65 list. To me, that was kind of a natural selection. And then I just kind of made my case for

including manganese.

And then the other compounds where there's evidence of carcinogenicity, those also kind of went onto my list. If I were to take anything off, it would be more to go in line with the CDC finding that they weren't coming up with any significant detections. And maybe that would be -- if we had to take something off, I would probably take those off, since they weren't finding them.

But at this point, given the laboratory capability, it seems like we're going to be measuring these anyway. And given kind of an interest and need for better assessment of mixed exposures, and what they mean -- might mean in terms of different sources of exposure and potential health effects, that this is an opportunity to kind of fill out our understanding of a range of materials that are commonly used economically and may interact in ways that we don't understand.

So I think understanding the individual and joint exposures is really valuable. So I see no reason to pare this down.

Dr. Quint.

PANEL MEMBER QUINT: Yeah. Julia Quint.

I went over the list too. And using the same criteria that my colleagues used more or less, I also was interested in the nanoparticles, the nanosizing of a lot

of these metals, because we right now don't have good criteria or measure -- or ways in which to determine whether or not, you know, these are causing increased adverse health effects. So I think, you know, just looking at whether or not they're increasing or whatever in the population would be also very useful.

So there weren't any -- I mean even barium, which to me doesn't make a -- there's not a good argument for toxicity, but if it's being used for drilling and for oil, then that, of course, it may become more important. So there weren't or any actually, when I think about it, that I would leave off. And the ones that CDC can't detect, I mean, your method of detection is -- you have a much sensitive method, because beryllium is really an important metal occupationally. So I would -- I guess I would go with Dr. Cranor's suggestion to list all of them as priority, unless down the line I get some indication that some should be left off.

PANEL MEMBER FIEHN: Oliver Fiehn.

I'm working now as an analytical chemist for more than 20 years, and I would not endorse a statement that I heard again that analytical chemistry is not an issue. I think this is a false statement. And analytical chemistry has very rigorous criteria. And I see here that in the QC references that we have been given today, I see here

coefficients of variation, I see, you know, 13 metals that I -- that have been shown to me that can be analyzed, but I don't see, you know, all of the chemicals.

And I say again, you know, I have not gotten -- received the impression that this has been all validated. And I think -- and that therefore, I cannot see that all of these has been shown to me that they are able to be analyzed at, you know, what we -- what some of the Panel members have thought they would hear, that it's all easy and, and all good, and all established, so -- and the reason is because seemingly it hasn't been asked so far of the lab to show.

So I am more skeptical -- and as an analytical chemist, I am more skeptical, until I see the data that it can be done -- that it actually can be done. Just because a method or an instrument is, in principle, capable to do things, that doesn't mean it actually be -- will be able to do these things, depending on all the different complications we've heard today, from transfer of -- from when we discussed chromium(VI) and chromium(III). Similar things, of course, are important for other metals.

Contamination issues. We have, you know, heard about contamination issues. So I am, you know, much less clear about the, you know, ability to measure all of these.

Now, this is only one of the criteria to designate compounds as priority chemicals, not -- you know, these were not like conjunctive, but they were not like "and". But, of course, if we ask, you know, the Biomonitoring Program to designate certain chemicals as priority, and then we say everything is priority, and then the laboratory is asked to do everything with, you know, an equal amount of scrutiny, then we have to think about like, you know, in terms of validation and contamination issues, will equal amounts of time be spent and who's paying for that?

I mean, you know, I am very much a friend of screening, and of screening more than one target at a time. You know, that's the idea of, well, broad profiling, if you like, to say that. And it's also okay if some target compounds will not be measured equally fine with equally low coefficients of variation than others, but I'd like to see the data.

And so I -- for myself, I can only vote to put those compounds onto the priority list for those that I have seen the data here. That was on slide number 9 in the presentation. Chromium, manganese, cobalt, arsenic, selenium, molybdenum, cadmium, mercury, thallium, lead, and uranium.

PANEL MEMBER QUINTANA: Cobalt?

PANEL MEMBER FIEHN: Cobalt is on there.

ACTING CHAIRPERSON BRADMAN: So just a clarifying question, Dr. Fiehn. So excluding the laboratory requirement, some of the ones that are missing from that like barium and antimony, would you feel that there's any public health or other consideration that would make them a priority or are you saying that you'd rather wait until the laboratory methods were validated before considering those as a priority?

PANEL MEMBER FIEHN: Yeah, we have heard before that, you know, due to inadequate methods and instrumentation, lots of old data are questionable. This was presented to us. And I'd like to avoid, you know, again producing non-validated data. So these are all designated chemicals anyway. So if the laboratory, you know, chooses then to say, well, since I'm on it, I will also look at antimony. That's fine, and I would encourage that to do so.

But there is always a difference between an internal view and an external view. And if State of California all of a sudden puts all of these compounds, including, you know, vanadium and others onto priority lists without having the validated methods, other states and other agencies might look at, "Oh, let's do it again", because they will -- may have also similar ways to look at

things.

And I'd like to say, let's have -- let's have methods first. If we -- let's encourage the laboratory to produce data that shows, yeah, this is our limit of detection, this is our coefficient of variation in this specific matrix, say blood and urine, which would make sense, because what's what you get from most of the specimen most of the time. I mean, you can't easily sample teeth. So, you know, as an analytical chemist, I would say that.

Now, from other criteria of exposures and, you know, sources of exposures, sources of toxicities, we all know that there's not much that is not toxic at some level. So, you know, I mean, it does matter if we're able to determine levels accordingly.

I would not go along with statements about the -- that was done by the Manganese Interest Group saying that the modeling is inadequate and you can't just take the blood plasma or serum as a model for exposure, because at the end of the day if we can measure it, and we are, you know, able to find differences, then we can link it to the sources, just as we had discussed before for chromium.

You know, so the idea then is, you know, can we link it to meta-data like exposure or occupational hazards and so on, once we have, you know, good ways to measure

it. Only then we can say, it's either related or not related to certain occupational hazards and so on. So I, you know, I just wanted to make a cautionary remark on the analytics.

ACTING CHAIRPERSON BRADMAN: Thank you. No. No, I think we appreciate the comments and understand it. I will mention though, I mean the Panel in the past in a different configuration we've taken a slightly different approach on these issues, but maybe we needed somebody with your background. But, for example, we recommended that diesel be a priority category for the State to biomonitor when we're at a place where we don't really even have a, you know, laboratory method or a biomarker for diesel. But we felt that diesel was an important exposure in California, and if and when the lab could develop or there's other resources to biomonitor diesel, we though it should be a priority to consider.

At the same time though, I am very sympathetic to the issues you're raising about, you know, not going too far forward without having the adequate laboratory resources in place.

So why don't we have perhaps last comments from -- individual comments from Dr. Kavanaugh-Lynch and then we can decide how we want to proceed as a Panel on whether we designate these as priorities.

PANEL MEMBER KAVANAUGH-LYNCH: So I have many of the same approaches to the lists that other members had. I, too, am most interested in those that -- that are on the Prop 65 list.

Another consideration that we have often -- that I thought we'd actually added to our list of criteria, because we're allowed to add, is the -- that it's of special interest to California. There's some reason why we would especially want to biomonitor it in California.

So I'm -- I mean, one approach is to say, yeah, there's -- there's rationale for several of these, so why not put the whole list on. There were some that -- to me, there wasn't much -- I didn't see much value in adding -- in calling a priority. For instance, I think it was -- yeah, the platinum, given that it's been not found in three cycles of the CDC. And I don't know of any special circumstances that would make that of special concern for California, like okay, I would -- you know, if I had to prioritize that, platinum would probably be at the bottom of my list.

So other ones that I didn't see a good reason for were uranium and barium. But on the other hand, I am particularly interested in antimony and beryllium. So those were my additional thoughts for what they're worth.

DR. GAJEK: May I address?

ACTING CHAIRPERSON BRADMAN: How about if we have Dr. Cranor and then Dr. Gajek.

PANEL MEMBER CRANOR: Two of us here.

ACTING CHAIRPERSON BRADMAN: Okay.

PANEL MEMBER CRANOR: One thing I failed to say -- Jenny picked up on one point -- you would expect to see higher exposures in working situations, and I think that's important.

The other place you would be concerned, I would think, for exposure would be in children. And so when these things have been identified for adverse health effects under Prop 65 or other studies, it seems to me that you want to look at the highly exposed populations and the vulnerable populations. And it seems to me that strengthens the argument for the toxicity side.

How much you're going to see there, I don't really know, but that's -- that would be the outcome of looking as opposed to deciding in advance.

ACTING CHAIRPERSON BRADMAN: Dr. Quintana, then a clarifying comment from Dr. Gajek.

PANEL MEMBER QUINTANA: I just had a couple of comments. One is maybe we should just formally go down and say which ones are on Prop 65 -- I was kind of circling them, but I'm not sure if I'm correct -- to make sure you say your favorite ones on Prop 65, but I'm not

sure I have the correct list in front of me.

ACTING CHAIRPERSON BRADMAN: Sure.

PANEL MEMBER QUINTANA: I'm circling them, but I think we should look at the CDC experience. For example, you said you're interested in antimony. And certainly in CDC and people exposed to secondhand smoke, and pregnant women exposed to secondhand smoke, you can see elevated antimony. And so if we have chemicals where we've seen differences in exposures we know are significant, I think that might be a reason to go forward, even if they weren't on the CV chart.

And I also wanted to ask the laboratory, maybe you can answer this now that I wasn't sure if that was all your data that was up there or just all that would fit on the slide, for example, and make sure we aren't overinterpreting from that one slide.

DR. GAJEK: These are urine -- metals in urine. We recently developed metals in serum. And almost all -- I mean, we analyzed for seven metals. And our detection limit in serum actually was plasma, was -- were in single digits. So for all these, we had a ppt level, single ppt level, so how good this method is.

And about analytical side of the story, I selected these metal not because I wanted, these were the most difficult to analyze. When you look at literature,

selenium, arsenic metals, they are very difficult. Ionization under plasma condition changes between 20 and 30 percent, so it limits the useful signal for these metals. Mercury is also considered as the most difficult, one of the most, manganese, chromium too. So I selected these metals for purpose. I make my life more difficult, not easier.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: So I think we've had enough discussion at this point. We want to be finished about now to be on time, so I think there's a couple of approaches we could take. We could go one by one and vote on these chemicals, or we can vote as a group. Are there any preferences in the Panel to consider one by one or group?

PANEL MEMBER FIEHN: I prefer one on one.

MS. HOOVER: Turn your mic on.

PANEL MEMBER FIEHN: I would, you know, argue for one by one for the reasons I outlined before, and because we had also arguments on different chemicals. So I think it would make sense to go, you know, through these metals that are under consideration today one by one.

ACTING CHAIRPERSON BRADMAN: Okay. Does anyone agree or disagree with that or should we just move ahead and do that?

PANEL MEMBER QUINTANA: Jenny Quintana. So to clarify, is the Prop 65 metals are antimony, beryllium, cesium, cobalt, platinum, and uranium? That's what I got just from this list.

DIRECTOR ALEXEEFF: Yeah, I don't think cesium and platinum.

PANEL MEMBER QUINTANA: Well, platinum is -- platinum says -- oh, it says platinum. Sorry. It says platinum. I just wondered did someone have the final list. So could you read off which ones there are.

ACTING CHAIRPERSON BRADMAN: Cesium is Prop 65.

MS. HOOVER: Stable cesium is not Prop 65. You have radioactive cesium, you have stable cesium.

ACTING CHAIRPERSON BRADMAN: Right.

MS. HOOVER: Again, in the interest of time, I want to make a proposal. So, first, you know, just really briefly, I'm not saying that analytical is not an issue. I'm saying that we need instruction, you know, from the Panel that you're interested in these metals, then we can put lab time -- lab and resources into it.

I was saying that we have a capable analyst who could do that work, but we need some guidance from you that you want that work done. Okay, that's number one.

Number two, I heard a number of people saying they're interested in putting the whole thing on the list.

You might want to consider making that motion, and seeing if it passes or fails --

ACTING CHAIRPERSON BRADMAN: I was actually thinking that way too, yeah.

MS. HOOVER: -- and then decide if you want to do a different approach, because to get into all the details of all -- each individual metal at this point, it's too late to do that at this stage. So we'd have to postpone consideration of one by one.

CAL/EPA DEPUTY DIRECTOR SOLOMON: This is Gina Solomon. I have just a -- if you wanted to breakdown into some subcategories, I have three possible subcategories to consider, but -- so maybe. Okay. We'll only do that, I guess, if the original motion fails.

All right.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: Okay. So I'm going to make a motion that, as a Panel, we consider all of the chemicals that were presented today as part of the potential designated -- the potential priority metals that we treat them as a group in terms of recommending one way or another as priority chemicals.

So why don't we take a vote on that, and --

PANEL MEMBER CRANOR: I will second it.

ACTING CHAIRPERSON BRADMAN: Okay. So we have a

second. So let's take a vote. Start on your --

PANEL MEMBER QUINTANA: What is a quorum for this Committee? I know we're short of members.

MS. HOOVER: Well, sorry. This is Sara again. Our lawyer is should be -- not here.

Okay. It's advisory only, this Panel. You don't need a quorum. So, you know, you can go ahead and take a vote and we'll take note of what that vote is. I mean, I'm happy to consider, you know, Gina's information. We could talk about different groupings, but we just would have to do that at another meeting. That's all I'm saying.

ACTING CHAIRPERSON BRADMAN: Okay. So let's decide, as a group, whether we want to go ahead and treat them as a group. Okay.

PANEL MEMBER CRANOR: You want a voice vote from each of us?

ACTING CHAIRPERSON BRADMAN: Yeah, I guess. Yeah.

PANEL MEMBER CRANOR: Treat it as a group.

ACTING CHAIRPERSON BRADMAN: Sure

PANEL MEMBER KAVANAUGH-LYNCH: I just have a question for Sara that I'll -- well, I just got it on.

So you want our advice on what direction -- on what things we're interested in, and -- but then you want us to vote yes or no whether we like this group or not? I

mean --

MS. HOOVER: I didn't raise that, as a possibility. Panel members raised that. Okay.

PANEL MEMBER KAVANAUGH-LYNCH: Okay.

MS. HOOVER: And then there's disagreement. And now we're just in the situation of we're out of time. I'm not saying I want you to vote yes on all, you know. I mean, ideally you would prioritize the priority metals and give us some guidance on what you think are most important.

So another option would be to defer at this time, you know, and just say we'll take it up at another meeting, and we'll go through it one by one or we'll go through groups, or we can, you know, cut some time out of, you know, something else a little bit later, cut break time, but we have to give, you know, our transcriber a break. Do you want to -- I mean, you could hear Gina's proposal for groups right now, since there seems to be disagreement on whether to even vote on all. So, Gina, why don't you go ahead and give your proposal.

PANEL MEMBER KAVANAUGH-LYNCH: Well, and my question is just to know what's most helpful to you, because that would change my vote.

(Laughter.)

MS. HOOVER: I mean, the way I envisioned it and

the way I presented it to Asa was that each member would say, you know, what -- which ones they considered to be priority, and they would give the argument as why. We heard some members do that and we had heard some members give a different opinion. So now we're just at the point of, you know, what the Panel, as a whole, would recommend. We've heard the individual recommendations.

So I'm pretty much open to what you would choose. Gina might have a proposal that would resonate with people, so why don't we go ahead and hear that.

ACTING CHAIRPERSON BRADMAN: Okay. Why don't we have Gina go through that, and then we'll decide to decide or decide to wait.

(Laughter.)

CAL/EPA DEPUTY DIRECTOR SOLOMON: Just in looking down this list, there -- I see three categories here. I see, you know, based on Dr. Fiehn's important observation about QCing and wanting to be sensitive to that, there are six chemicals here that are on the QC list, cobalt, manganese, molybdenum, thallium, tungsten, and uranium. And all of those have some very significant toxicity concerns. And so that seems to be one group that might, you know, be considered.

There's another group that has -- is neither on the list of chemicals that has been QC'd, nor do they

flag, at least in my mind, really strong toxicity concerns. And at least a couple of those have been mentioned, barium, cesium, and platinum are probably the lowest toxicity of the chemicals on this list.

And they haven't yet been QC'd. So those might be, you know, ones to consider a little separately. And then there are two that fall in a middle category, antimony and beryllium. These have not been QC'd. However, it's a very high expectation that they would pass QC, and they are of some interest from a toxicity perspective. And so those might be considered -- you know, the Panel might consider whether those should be brought back or identified now as priorities or considered for priority for developing this kind of QC data.

ACTING CHAIRPERSON BRADMAN: Gina. Dr. Solomon, thank you. That was very helpful.

MS. HOOVER: I'll just put the whole list back up and you can -- let's see, where are we here?

Okay. So, yeah, given what Gina just presented and what others have said, why don't you just pick off a proposal based on that.

ACTING CHAIRPERSON BRADMAN: Okay. I think what I'm going to do -- are there comments on the left wing that has --

(Laughter.)

ACTING CHAIRPERSON BRADMAN: Okay. So, Gina, I think that was actually very helpful to put those. And I think it kind of reflects some of the discussion here. It's nice to have an outside view. So I think what I propose is that given earlier statements among several of us that we were interested in potentially the entire list, that first proposal for a motion would be that we designate the six with adequate QA/QC as priority chemicals.

Okay. I see some nods, so let's use the appropriate language for that and then make a motion. So Dr. Bradman motions that the six chemicals that we discussed with adequate QA/QC data so far, including cobalt, manganese, molybdenum, thallium, tungsten, and uranium be included as priority chemicals in the California Environmental Contaminant Biomonitoring Program.

Is there anyone who'd like second that?

PANEL MEMBER QUINTANA: Dr. Quintana will second that motion.

PANEL MEMBER FIEHN: I second.

ACTING CHAIRPERSON BRADMAN: Okay. We have a second and a third.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: So why don't we

start on this end, on the right wing today and then we'll come down.

PANEL MEMBER KAVANAUGH-LYNCH: Aye.

PANEL MEMBER FIEHN: Aye.

PANEL MEMBER QUINT: Aye.

ACTING CHAIRPERSON BRADMAN: Aye.

PANEL MEMBER QUINTANA: Aye.

PANEL MEMBER CRANOR: Aye.

ACTING CHAIRPERSON BRADMAN: Okay. So we have unanimously recommended that these -- six of these metals those, those just mentioned are -- should be priority chemicals for the Biomonitoring Program. Now, I want to consider whether we should propose antimony and beryllium. Those came up specifically in the public comments and in some comments by Dr. Quint, in terms of occupational exposure. And I wanted to ask if anyone in the group would like to propose those two as priority chemicals?

Dr. Kavanaugh-Lynch.

PANEL MEMBER KAVANAUGH-LYNCH: I move that we put them on the list with the caveat or encouragement to develop the QC to make those levels believable.

ACTING CHAIRPERSON BRADMAN: Can I rephrase that?

PANEL MEMBER KAVANAUGH-LYNCH: Yes, please.

ACTING CHAIRPERSON BRADMAN: Okay. So Dr. Kavanaugh-Lynch motions that antimony and beryllium be

included as a priority chemical in the California Environmental Contaminant Biomonitoring Program contingent on adequate QA/QC standards that meets the Program goals. Okay.

PANEL MEMBER KAVANAUGH-LYNCH: Yes, I would.

ACTING CHAIRPERSON BRADMAN: Would anyone like to second that?

PANEL MEMBER QUINT: I'll second.

PANEL MEMBER CRANOR: Second with a comment. I concur. I'll second. I was on the oversight committee for Los Alamos Labs a number of years ago, and I was in on a discussion of beryllium. They were very concerned about beryllium, because it's a very lightweight metal, easily -- you know, it takes very little in terms of exposure, so that clearly ought to be in there. I don't know about antimony, but I support the motion.

ACTING CHAIRPERSON BRADMAN: Okay. Thank you. Okay. So that leaves -- I want to thank Gina again for providing some order to this. Do we need any discussion for barium, cesium, and platinum?

DIRECTOR ALEXEEFF: You didn't vote on that.

ACTING CHAIRPERSON BRADMAN: Oh, I'm sorry.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: I guess I know how I'm going to vote.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: I am the Acting Chair today.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: All right. Well, let's start -- we'll start on the left wing for this vote.

PANEL MEMBER CRANOR: Yes. I vote yes for the two additions.

PANEL MEMBER QUINTANA: Aye.

ACTING CHAIRPERSON BRADMAN: Yes.

PANEL MEMBER QUINT: What are we voting on?

ACTING CHAIRPERSON BRADMAN: We're voting for the putting the two, antimony and beryllium.

PANEL MEMBER QUINTANA: Yes.

PANEL MEMBER FIEHN: Yes.

PANEL MEMBER KAVANAUGH-LYNCH: Yes.

ACTING CHAIRPERSON BRADMAN: Thank you. So that passed. So antimony and beryllium are also recommended as priority chemicals for the Biomonitoring Program.

PANEL MEMBER CRANOR: Did you say barium or beryllium?

ACTING CHAIRPERSON BRADMAN: Beryllium.

MS. HOOVER: Beryllium. Why don't I just read for the record. So the Panel has now voted to recommend as priority chemicals antimony, beryllium, cobalt,

manganese, molybdenum, thallium, tungsten, and uranium.

ACTING CHAIRPERSON BRADMAN: Correct.

Okay. In the interest of time, do we want to have any additional discussion about the other three compounds, barium, cesium, and platinum or maybe we'll defer that to another meeting.

ACTING CHAIRPERSON BRADMAN: So based on the nods, I think we'll wait on those three.

MS. HOOVER: Great. Thank you. And thank you, Gina, for bringing this item to a close.

One last slide I want to show you, if I can get my slideshow back. Sorry.

So the last thing I want to just put a pitch in, as you can see this is very difficult. And so after today's meeting, we'd really like the Panel members and the public to take a look at the metals that will be newly designated in April 2014, which is in your materials, review the periodic table, send any suggestions to the Program on metals that you would like to see or groups of metals for possible future consideration as either designated or priority chemicals.

And given it's 3:00, we still need a 15 minute break, so we'll start back promptly at 3:15.

ACTING CHAIRPERSON BRADMAN: Actually, I was going to suggest we cut it to ten minutes or must it be

15?

MS. HOOVER: You can try, sure. 3:10.

ACTING CHAIRPERSON BRADMAN: Yeah. Everyone, please be back promptly at 3:10.

Thank you.

(Off record: 3:00 PM)

(Thereupon a recess was taken.)

(On record: 3:11 PM)

ACTING CHAIRPERSON BRADMAN: It's about -- it's a little after 3:10, so we wanted to get started. We're going to get started now.

So thank you. I think we are now ready to get started again. Thank you for taking a shorter break. I want to mention that Dr. Cranor had to leave early to catch a plane, so we're going to miss his participation during the next session.

So I want to welcome everyone back. And then we're now going to hear I think what would be a very interesting presentation on, "Best Practices for Biomarker Collection, Analysis, and Interpretation - Perspectives from U.S. EPA's Chemical Safety for Sustainability Research Program", by Dr. Jon Sobus. And those of you who had a chance to look at some of the materials posted earlier, I think this will be a very interesting presentation. I'm looking forward to hearing that.

We are starting a little bit late, but I think we're -- we should be on time to be able to end on time, if we go through the presentation quickly and -- anyway, stay within the constraints.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: So anyway, I don't know, Sara, if you're going to introduce Dr. Sobus?

MS. HOOVER: Yes, I will.

ACTING CHAIRPERSON BRADMAN: Okay. Thank you.

MS. HOOVER: Yes, I will.

Yeah, so -- thanks, everyone for getting back in time. Dr. Jon Sobus, I can't take credit for bringing him here. He actually called me out of the blue and he had been instructed by one of his managers to reach out to the State biomonitoring programs. And he called me and we had a great chat. And I said, "Hey, come to the SGP meeting".

And we had a really wonderful meeting yesterday with the labs, ECL and EHL, and we've had a lot of really fruitful discussion. So I'm really, really happy to have made this connection with Jon.

So Dr. Sobus is a physical scientist in U.S. EPA's National Exposure Research Laboratory in Research Triangle Park in North Carolina. He's a member of the graduate faculty at UNC Chapel Hill, in the School of Public Health.

At EPA, Dr. Sobus serves as a project leader for biomarkers research under the Chemical Safety for Sustainability research program. His roles are to foster biomarkers, research collaborations, and manage research that will lead to the increased use of biomarker data to support regulatory decisions and actions.

Dr. Sobus's specific research activities include field monitoring to evaluate human exposure to VOCs and SVOCs; laboratory analysis of blood, breath, and urine for specific chemical analytes; analysis of complex datasets using statistical models; and, exposure/dose estimation of target chemicals using PBPK models. He received his B.S. in Environmental Health Science from Salisbury University, and his Ph.D. in Environmental Science and Engineering from UNC Chapel Hill.

Dr. Sobus.

(Thereupon an overhead presentation was presented as follows.).

(Applause.)

DR. SOBUS: Thank you, Sara for the very, very nice introduction, and thank you again so much for being so receptive to me participating in this great function today. And thank you for the hospitality that you've shown over the last several days. It's been really great being here. It's great to participate. It's really been

awesome to come here and learn about some of the stuff that's happening in the State. I've had the opportunity yesterday to meet with a lot of really great scientists to tour some excellent lab facilities. There's some terrific equipment, some great work being done, and it's really excellent to learn about this and take some of this information back to the EPA where I am in RTP.

So Sara said I've currently been a project leader for this activity called Chemical Safety for Sustainability Research Program. And there's a couple specific research projects that really focus on using biomarker data and collecting new biomarker data. So I wanted to come today and talk about some of the innovative things we're doing for biomarker collection, analysis, and interpretation.

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DR. SOBUS: So a brief outline of the talk today. I just want to give some orientation on our different lab centers and research programs. And then the bulk of the talk will be on our specific biomarkers research projects.

There's two real projects that I'll talk about today, and this represents a very small percentage of our overall research portfolio as it relates to biomarkers. But I'll talk about how we're focusing on looking at how existing biomarker data is being used and thinking about

how we can potentially come up with some new uses of this. And we're doing this through computational case studies.

And then we've also thought about how we can go about collecting samples a little bit intelligently and making some new measurements of some chemicals that we haven't really looked at before. So I'll talk about one particular biomonitoring field study today as well. And then hopefully I can summarize this stuff with some take-home points. And hopefully, the talk today will be relevant to the discussions that we've heard earlier today.

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DR. SOBUS: So this is where I work. This is the EPA facility in Research Triangle Park, North Carolina. It's a fairly large facility. I believe we have several thousand employees here. It's a large campus that we share with the National Institutes of Environmental Health Sciences. They're located right across the lake on this side.

And I just wanted to give you some flavor for what makes up the Office of Research and Development. Basically, we have three research laboratories, the Exposure Lab, the Effects Lab, and the Engineering Lab. And then we have four research centers that are focused on homeland security, environmental risk assessment,

computational toxicology, and then extramural research.

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DR. SOBUS: So ORD's main function is to conduct research and to support research that will ultimately support regulatory decisions and actions. And probably about four or five years ago, we realigned our research portfolio to these six key research programs. And they focus on Air, Climate, and Energy; Chemical Safety for Sustainability; Sustainable and Healthy Communities; Safe and Sustainable Water Resources; Homeland Security; and Human Health Risk Assessment.

And really the goal here is to take scientists in the different labs and centers and have them do integrated work on these different research programs. And I've highlighted the Chemical Safety for Sustainability Program, because the work I'll describe here today has been captured under that research program.

Now, again, that by no means means that biomarkers research isn't done in the other programs, cause it certainly is. So again, this is a small piece of research that I'll be covering today.

But the goals across all these different research programs is to really focus on integration, doing innovative research, and focusing on sustainability.

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DR. SOBUS: So when the CSS Research Program was first conceived, we basically thought of it as two projects. One project, that was to focus on the near-term work, was basically looking at what data is out there with respect to biomarkers, and then looking at the different techniques for evaluating that data and interpreting it to support regulatory decisions and actions.

So we really thought about three goals for this project. One was to look at what data is out there, and to look at how it's being used. Two was to look at some of the challenges in interpreting that data from a risk assessment standpoint, and really highlighting what the critical data gaps might be. And then third was to think about how we can propose new methods on the same data that would be particularly innovative, and then, based on case studies, recommend best practices for doing similar analyses.

So this is some of the work we've been doing over the past year, year and a half in some of the case studies that I'll present today.

The second project -- they started at the same time, but this is really meant to be a longer term project, and to some extent a continuation on project one. And the goal here is to actually conduct some studies, so human observational studies, as well as animal

experimentation, because this -- as you will see, this project is made up of scientists across the Exposure Lab, the Effects Lab, and the Computational Toxicology Center, but to perform some new studies to identify new biomarkers.

So now we're extending what can we do with existing data to how do we go about collecting new data and looking for new biomarkers. And I won't get into too much of this discussion today, but we're really starting to think about some of the discussion earlier today pertaining to this. You know, how do you extend beyond just the targeted chemicals that we've been looking for? And how do we develop models to make predictions for chemicals where we don't have a lot of data?

So can we go about collecting targeted biomarker data to support model evaluation? And then if we don't have current models, how can we use biomarker data to develop new models or maybe even refine some of the existing models?

So this is just a flavor for the two projects. And I'll start today by talking about some of the case studies we're doing for project one.

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DR. SOBUS: We have a fairly good sized group, again, of members from the Exposure Lab, which is these

group of individuals, the Health Effects Lab, this is our National Center for Environmental Assessment, and then our Computational Toxicology Center.

I will say that, you know, all of these are active participants on the study, but a lot of people split their time across different research projects.

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DR. SOBUS: So we started by saying, you know, what are the biomarker data that's being used? And as a first pass, we decided to focus on the NHANES data, because this is the largest source of biomonitoring data in the country. Now, certainly all the case studies that we've performed would be applicable to local and state surveys as well, and other small and large studies.

But we just wanted to get a handle on, you know, how much data is out there, how is it being used? So the first thing we did, as you can see in the figure on the left-hand side here, is we went in and we did a simple PubMed search looking for publications that had the acronym NHANES in the title or abstract starting from 1999 and we ended this search in 2012.

And we basically saw that in 1999 there was about 50 papers that appeared to be using the NHANES data. And as you can see, there's been a very clear and sharp increase over time, so that in 2012, there was over 400

papers in this PubMed search that used the NHANES data. So we know there's a real increase in the use of this publicly available data, but the question was how much of it is being used to evaluate biomarkers of chemicals?

So we went in, and we did a manual curation of these papers, and we basically calculated percentages for each year of how many of these papers were focusing on biomarkers of environmental chemicals. As you can see, the percentage was fairly low in the early years. It hung around five percent and then it's kind of steadily rose now to over 15 percent, and I believe it's continuing to grow now.

So we can say that there's an increased awareness and use of the data, and there's an increased focus on looking at these biomarkers of environmental chemicals.

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DR. SOBUS: So the next question is what are people doing with it? So when we aggregate the results from this NHANES lit review, we found there was about 3,000 papers that appeared to be using the NHANES data. Upon manual curation, we found that about 2,600 weren't focusing on biomarkers at all. They were just looking at nutrition or health endpoints. And only about ten percent were actually focused on the chemical biomarker data.

So we further broke it down into applications of

the data or evaluations of the data using different techniques. We found that about 20 percent used, what I would call, descriptive techniques. And I think this was the intended use of the NHANES data.

This is where you're comparing biomarker measurements over time to look for trends or comparing across subpopulations or looking to see if there's been a decrease in biomarker levels as a result of a risk mitigation strategy, or for example, maybe comparing biomarker results from a state survey to the NHANES data. I would classify those all as descriptive.

So again, we're looking at about 20 percent of the papers that did that approach that -- you know, where the NHANES is really intended to support. There was a slightly smaller percentage that performed, what I called, risk-based evaluations. So here, you're actually comparing the biomarker measurement to some value that's a risk-based reference level. And that can be based on an external exposure or an actual biomarker concentration.

So when biomarkers from the NHANES are compared to a biomarker-based reference level, we would call that direct use. And there's very limited application of that technique as there's very few biomarker-based reference levels, such as blood lead.

So the bulk of these risk-based studies performed

modeling evaluations. And we can think of that either as a forward evaluation or as a reverse evaluation. So for the forward evaluation, you essentially start with a reference dose or some other value that's based on external exposure, and you predict a biomarker concentration that would be consistent with that reference dose.

This is something now that's being called biomonitoring equivalents, and it's been applied to many chemicals. So you then predict the biomonitoring equivalent and compare it to the distribution of biomarker measurements from the NHANES. And you can say something about exposures relative to the biomonitoring equivalent in the form of a hazard quotient or margin of exposure. So that's one method.

The other method is the reverse application, where you take the biomarker measurements and you reconstruct to figure out what the exposures could have been that led to the biomarker level, and then you compare that to the reference level of interest. So this represents basically the smallest use, but still a pretty good use of the NHANES data. But by far, most of the publications were, what I would call, association-based studies, where you're looking at the relationship between a biomarker and something else, be it a health endpoint or

some predictor of exposure.

So we can break it out and say, you know, some percentage -- actually a very small percentage are exposure focused. So different exposure factors in the NHANES data would be used to predict the biomarker concentration to say these are the things that drive exposure.

So a fairly small percentage actually were, what we called, exposure focused. The bulk were health focused. So they were saying, this biomarker concentration is predictive of this health endpoint. And then when we further broke out that category to say, you know, how are these health focused studies being conducted, the very large, overwhelming majority, 116 out 120 studies were targeted in the sense they compared one or a few chemicals with basically one endpoint. So very targeted evaluations with *a priori* hypotheses being tested.

A small number, and these were all very recent papers, were what we called semi-targeted or semi-supervised studies, where more biomarkers were compared to more disease endpoints. And I'll talk a little bit about that in the upcoming slides.

But this was basically our map for what's being done with the existing data. And we've kind of said given

the state of the science, what other work could we do specifically to advance some the risk-based studies and some of the association-based studies?

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DR. SOBUS: So I'll talk in depth about two case studies and then briefly mention a few others. The first case study that we focused on wanted to kind of look at these association-based research endeavors. A colleague of mine in NCEA, Krista Christensen, came up with the observation that -- she was looking at the relationship between phthalates and measures of body size, she was getting different results in her epidemiological models, and we wanted to comment on that.

So we put together this study. We've now submitted a paper to Environment International. And the title of the paper was, "Changes in epidemiologic associations with different exposure metrics: A case study of phthalate exposure associations with body mass index and waist circumference."

So again, we kind of had this observation that when you build these epidemiologic models, you have the option to pick different exposure surrogates for a particular biomarker. So, for example, if you have a urine biomarker, you can do urinary concentration or creatinine-adjusted concentration.

And we found that depending on which one you pick, you get a different answer in your epi model. So the question is which one is more right, or which one is less wrong?

So ultimately, what we wanted to know with this case study is, can we define and recommend best practices for picking an exposure metric for any epi model?

So how did we go about doing that?

Well, the first thing we did was we looked at the NHANES data and we calculated as many different exposure metrics as we could for given phthalates. And then we looked at the association between those exposure surrogate levels and waist circumference and body mass index. So that tells us the variation in results, but it doesn't again tell us which one is most correct.

So we had to do a simulation experiment, where we basically gave random exposures to the same NHANES individuals and then looked for associations based on those random exposures. And then we compared results of the simulation to results of the actual NHANES analysis to try and learn some lessons and then recommend best practices.

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DR. SOBUS: So it's a little hard to see, so I'll walk you through it, but this is the results just using

the body mass index models. So we have here, for each of these columns, the regression coefficients and standard errors for five different exposure metrics. So we have the first exposure metric is given in molar excretion rate, so nanomoles per minute. The second is molar concentration, nanomoles per ml. The third is concentration, but including creatinine as an independent variable in the model. This is something that's done quite frequently now. The fourth is doing just a creatinine-adjusted concentration measure. And the fifth is doing a reconstructed intake that's adjusted for body weight. So we have these five different exposure surrogates that all originated from the same biomarker level, and we did regressions for the different phthalates with the outcome being the body mass index.

So if you look down for a given exposure metric, you can see that the results are very consistent across the different phthalates. For the excretion rate, we basically have strong positive effect across the board. When we move over to concentration, the effect is a little bit stronger.

When we move over to the models that had creatinine as an independent variable, the association is a little bit weaker. Again, they're all in the positive direction, but we're seeing some change in the

significance.

This gets interesting. When you move over to the creatinine-adjusted value, the effects are no longer significant at the 0.05 level. And then when we move all the way over into the reconstructed daily intake, extremely significant. So not a lot of difference in the models across the different phthalates, but pretty large differences, at least as far as interpretation goes, as you move across the different exposure metrics.

So here we demonstrated the variability in the results, given what you might find. I also want to point out, this is only really a capability to do a lot of this stuff in the '09 and '10 NHANES data, because they started collecting full volumes of the void and reporting that.

And I'll show that in the next slide. You couldn't do this type of analysis on earlier data, where they didn't have full void volumes and the time of the void.

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DR. SOBUS: Okay. So I hope I've convinced you that you have some variation in the results depending on your exposure metric. So now we're trying to get at which one may be the most correct, or at a minimum, the least biased. So this is a complicated figure. I'll walk you through it.

Essentially, again, what we tried to do was take as much of that same NHANES data as we could, so the body mass index, the waist circumference, and all the other meta-data that you basically see up here in the red ovals. But we threw away the biomarker concentrations, and instead we started with the distribution of dietary exposure that we got from a paper, Fromme et al. in 2007. And we randomly assigned those dietary exposures to the NHANES subjects.

So based on that random assignment, there should be no association between the randomly assigned phthalate exposure and the outcome of interest. I hope you can all believe that. And we did test it, and there was no association. So that was our starting point.

So basically what we're looking at is as you go down the line and calculate the different exposure metrics, if you see an association, it's demonstrating that you've introduced bias, and the magnitude of the regression coefficient says how much bias there is. And ultimately that tells us which ones do we not want to pick.

So this is how we did it, and I think this was pretty clever. Again, we took the random intake and we put it into a PBPK -- or a PK model, sorry, for DEHP that published by Matt Lorber in 2010. We needed a couple

parameters to go into the model. We needed the weight, which we could get from the NHANES, and we needed the time of the void. Now, the NHANES will only give you three different MEC sessions. They will not give you the specific time of the void. So we took the MEC session and we randomly selected a time for that subject, but we also needed the time of the previous void.

We could get that by taking the urine volume and the urine output that is now given in the 2009-2010 NHANES, and we calculated the time since the last void. So we put that into the model. And all that combined information right here allowed us to calculate the chemical excretion for all the NHANES subjects. So it's a totally made up value, but it should be independent of BMI and waist circumference.

So that's really our first calculated exposure metric, but we wanted to get the others. So when we took chemical excretion and we coupled it with urine output, again from the NHANES, we got chemical concentration.

When we took the excretion and coupled it with creatinine excretion rate, we got the creatinine-adjusted concentration. And when we coupled that with the creatinine excretion model of Dave Mage from 2008, we could predict the daily reconstructed intake. So through this series of simulations, we were able to get the

original exposure metric, the truth as we assigned it, and these four other exposure metrics that may or may not be biased.

So the goal was then to run the same epi models adjusting for the same parameters, age, sex, race, ethnicity, poverty index to see if we got similar results to what we saw with the actual NHANES data.

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DR. SOBUS: And without showing a lot of coefficients and P values, these are the results. So I'll remind you what we saw with the NHANES data, we virtually had no effect when we looked at creatinine-adjusted concentrations. We had significant positive effects with excretion rate and concentration values, and then we had these really, really strong positive effects of the reconstructed daily intake. And again, at the time, we said we don't know which one is right.

Well, here's the simulation results. As expected, there was no effect of random intake on BMI and waist circumference. There was also no effect of concentration and excretion rate on that outcome variable. So from that, I would stop right here and say, you know, concentration excretion rates are probably the least biased exposure surrogates for this particular analysis.

But interestingly, we saw that the

creatinine-adjusted values, whether it be an independent variable in the model or an outright adjustment in the denominator, we saw significant negative effects between the exposure surrogates and the outcomes of interest, that completely demonstrates a negative bias that's been introduced by the meta-data.

Then on the complete opposite side, we saw the significant positive effect of the reconstructed daily intake. Again, there should be no association, given that there was no relationship between the true exposure and the outcome variables of interest.

And I think what was most fascinating about this is when you look at the order of these effects, you're seeing the exact same order in the simulation results as you're seeing down here in the NHANES results. The only difference is these are shifted to the right. So that tells me the fact that this has shifted to the right, there could be something going on, some underlying positive effect between the chemical exposure and the outcome of interest.

But the fact that you're seeing this disparity across the different exposure metrics being reflected in the simulation, clearly indicates where some of this bias is coming from. So we tried to, in the paper -- and I won't get into it today -- kind of generalize this

procedure and recommend simpler procedures, so you don't have to get into very difficult PBPK type simulations. We're basically evaluating which exposure surrogate might be the least biased and therefore most preferable for a given epi study. So again, hopefully that paper will be accepted in short order and something we can share with everyone.

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DR. SOBUS: Okay. So switching gears from the association-based studies to risk-based studies. So again, now we're talking about comparing biomarker measurements from the NHANES or anything else to a risk-based reference level, typically based on external exposure.

So this was a study led by Joachim Pleil. He's in our National Exposure Research Laboratory. This has actually been published. This is the first paper that's been published as part of our team. This was published in the Journal of Toxicology and Environmental Health, Part A fairly recently.

The title of this paper was, "Estimating lifetime risk from spot biomarker data and intraclass correlation coefficients". Now, we have shared this paper with group, I believe. There's some math. So if anyone wants more detail, they can certainly go to the paper and I'm happy

to talk to you about it afterwards.

But this was a really tricky problem. Basically -- and this really focuses on nonpersistent chemicals, but you've got these spot biomarker data in the majority of studies, particularly the NHANES, where one sample is collected from one person. Yet, the risk-based reference levels are determined based on long-term exposure, in most cases. So you've really got this apples to oranges comparison. You know, how do you fairly compare spot measurements to long-term average based reference levels?

Ultimately, what we want to know here is what percent of the population has long-term exposure above a reference level? That's the ultimate science question here. So to get at that, we first had to develop an approach that would convert a distribution of spot samples to a distribution of averages. Once we do that, we can calculate population exceedance based on average biomarker levels that would be above the reference level. And then finally, we can develop a tool, so that people can actually take information from places like NHANES or from Biomonitoring California, plug in some statistical parameters, and calculate these exceedance values for any chemicals that they want. So hopefully, I can convince you here that we've done that successfully.

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DR. SOBUS: So to do this, we had to actually start with some real data. So this was hydroxypyrene data that I provided. It was 220 observations from a group of individuals with a known geometric mean and geometric standard deviation. And essentially, this was our starting point.

We wound up, and we detail this in the paper, kind of bootstrapping this, adding the number of observations, and then assigning repeated observations to individuals. And the goal was we wanted to manufacture different groupings of repeated observations, in order to calculate something called the intraclass correlation coefficient. And I'll give a little statistic tutorial.

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DR. SOBUS: The intraclass correlation coefficient is essentially something called the between-subject variance component divided by the total variance. So the between-subject variance measures the difference in average biomarker levels across individuals in a population. The within-person variance component basically measures variability in repeated measurements for an individual over time. So the ICC has a possible range from zero to one.

Now, if there's no difference on average between

individuals in a population, we would say there's very little between-subject variance, sigma square B is going to be very near zero, and thus ICC is going to be very near zero.

On the flip side, if everyone on average is very different, but repeated measurements for an individual are all very similar, we would say that sigma squared W is near zero and thus ICC is near one. So what we did is we took that original data set, and we bootstrapped it, and we manufactured different groupings of the biomarker measurements to generate all these different ICCs. And then we built some mathematical models and used that data for calibration. And again, I can't really get into that today, but it's in the paper if you're interested.

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DR. SOBUS: This was the output of all that mathematics. These are five generated distributions of average biomarker levels that are all based on that original distribution of spot samples. And I'll first draw your attention to the green line. It's a little bit hard to see, but the green line represents the predicted distribution under the condition where the ICC equals one. So this says all of the variability in the biomarker measurements are between subjects on average. There is no variation within a subject.

In other words, if you were to take one observation from one individual, that would be a very good or perfect reflection of that person's average biomarker level over time. So this is something we see more often with persistent chemical biomarkers, not so much nonpersistent chemical biomarkers. So we only show five distributions here, but we can do this for any value of ICC. And you can see that as ICC goes from 0.75 to 0.25, or from 0.5 to 0.25 to zero, you have this tightening of the distribution, such that more area is under this peak, and less area is under the tail. So why is this phenomenon important?

Well, let's say we have some biomonitoring equivalent value out here. I will say, this is not a value that we calculated. We just picked it out of convenience to illustrate this point and the method.

So if we blowup the area to the right of this BE level, we'll see something like this.

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DR. SOBUS: So what we want to do here is calculate the area under the curve to the right of the BE, and that basically represents the percentage of the population that generated the biomarker measurements that would be in exceedance of a biomonitoring equivalent or some value in biomarker space that's consistent with a

reference exposure level.

As you can see that when ICC equals zero, there's no area under the curve. So, on average, no one would be exceeding this BE. Perhaps in spot samples they would be exceeding the BE, but not on average. And then as you go up from ICC equals 0.25, 0.5, 0.75, and 1, you can see there's more and more area under the curve.

So you can see here that ICC is really driving what percentage of the population would be expected to exceed the BE on average. So assuming that risk is proportional to long-term exposure, we would say that in this scenario up here, we have less risk and in this scenario we have more risk.

So again, I'll turn your attention to the paper, because I don't have time to get into it, but we did generate a tool in Excel, where if you have a geometric mean, a geometric standard deviation, an estimate of the intraclass correlation coefficient, a number of repeated observations, and some BE value or any other value of interest, you can do these calculations for any chemical that you want. And we're happy to share that tool with anyone.

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DR. SOBUS: Okay. So I took a little bit of time on those. I just wanted to kind of briefly go through a

couple other kind of interesting case studies that we've been performing. With respect to the association-based studies, one of the things we found, particularly for the nonpersistent chemicals, is there's very limited standards for doing analyses and for reporting those analyses.

So if you go in and you target a study and look for epi relationships between a nonpersistent chemical biomarker and an outcome, there's very little guidance for how to do that work, you know, how to evaluate the biomarker itself, and how to report that.

So Judy LaKind put together a workshop made up of experts in different fields, so epidemiologists, analytical chemists, biomarker specialists. And we basically came up with this proposal for assessing study quality. And this is meant to be an instrument for individuals reviewing research proposals, manuscript submissions -- we're doing weight of evidence assessments.

And we called this instrument the, "Biomonitoring, Environmental Epidemiology and Short-Lived Chemicals Instrument." And again, the goal here is to have something for doing systematic evaluations of these association-based studies with the focus on the nonpersistent chemical biomarkers.

So I'd be happy to follow up with anyone about that, as would Judy, but this has been submitted to

Environment International.

The third challenge for association-based studies that I'll talk about -- and I'll reference back to our review slide, where we basically showed like 116 studies did targeted association-based studies where four did semi-supervised studies. We can probably be a little bit more thoughtful about this than doing just one chemical and outcome at a time, that there's limitations to using the traditional regression-based models for doing multiple testing, because you have to then adjust for multiple testing to guard against false positives.

So a few of my colleagues in the health laboratory -- or the Effects Laboratory, Shannon Bell and Steve Edwards, came up with the idea of using frequent itemset mining, a tool used in market-basket surveys, and applying that to the NHANES data to basically look across all environmental stressors and to look across all outcomes, and then to prioritize association based on the strength of association.

And this method actually gives you odd ratio estimates. So they published the method, and they're currently in the process of applying it to NHANES data going back several years.

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DR. SOBUS: The last study that I'll talk about

pertains to the risk-based evaluations. The distributions I showed before in comparisons to the BE are an excellent tool for looking at the population, what percentage of the population would be exceeding BE, but we also had interest in looking at individuals, and that's something that that's been done before.

So it occurred to us that biomonitoring equivalents are very useful pieces of information, but there's not necessarily one biomarker concentration that would be expected given exposure at a reference level. These things vary over time, so there's likely many biomarker concentrations that you could observe if you randomly selected from an individual that had been exposed at a reference level.

So the first thing we did for this study was figure out how to generate a distribution of biomonitoring equivalents. Then we statistically evaluated that predicted distribution with observations of NHANES biomarkers and we came up with a statistical interpretation at the individual level, which was basically the probability that any individual had been exposed anywhere near the reference level.

So the goal of this evaluation was to basically take the biomonitoring equivalent approach and start to bring it to the individual level for interpretation. So

this is a paper that was submitted to Regulatory Toxicology and Pharmacology. And we just were notified a few days ago it has been conditionally accepted.

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DR. SOBUS: Okay. How am I doing on time?

ACTING CHAIRPERSON BRADMAN: Ten more minutes.

DR. SOBUS: Great. So I'm going to completely switch gears. I'm hoping this next bit of the talk is relevant. So far, we've been focusing on project one, which is, you know, trying to think of new ways to use existing data.

This part is how do we go about collecting samples in new ways, getting more information. And I hope this is relevant. I heard about so many good studies that you all are involved with in leading. I hope this is relevant information to your work.

So about four or five years ago, we started conducting this, what we call, the Exposure Reconstruction, or Ex-R, Study. The goal here was to, A, focus on urinary pyrethroid metabolites, but to really carefully assess the variability in these biomarker levels for non-occupationally exposed adults over a six-week period of time.

We generated massive amounts of samples, as you will see. And the ultimate goal was to use these massive

amounts of samples and data that we are generating to accurately estimate exposure and absorbed doses using mathematical exposure reconstruction approaches.

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DR. SOBUS: So this was a fairly large team. The principal investigator was Marsha Morgan at EPA. I was a part of the field team and the analytical team and we were in the field for, I believe, a couple years. But again, a fairly large effort that spanned a fairly decent chunk of time.

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DR. SOBUS: So some specific study info. This study took place both at the EPA Human Studies Facility in Chapel Hill, North Carolina, in addition to participant's homes, which had to be within a 40-mile radius of the facility.

We recruited 50 adult subjects ages 18 to 50, and each participant was actively engaged in the study for a six-week monitoring period. Specifically, they provided samples and filled out questionnaires during weeks one, two, and six of the study.

So from them, we had them fill out food diaries, activity diaries, and pesticide use diaries. We collected duplicate solid food samples, a drinking water sample, a surface wipe samples, dust, and many, many, many urine

samples.

The primary sample analysis has focused on pyrethroids and metabolites, but this has been expanded to include other chemicals through partnerships with CDC and through internal analyses. The field study duration started November 2009, ended May 2011, and we're just now starting to see some of the chemical biomarker data coming back in.

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DR. SOBUS: So I want to give you a handle on basically what a typical week looked like for the participants. On days one and two, we got duplicate diets of the breakfast, lunch, and dinner. Starting at the end of day one with the bedtime void, we got -- and these are all full voids, full volumes. We got the bedtime void, every void on day two through the first morning void on day three, and then we repeated that procedure at the end of the week.

We got a surface wipe sample every day four. We got one vacuum dust sample only in week six. And we got one drinking water sample only in week six. But we had diary information for both food intake and activities virtually for every day that we did sampling with the exception of days where subjects would come to the clinic to swap out kits.

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DR. SOBUS: So when I say kits, I mean these. We basically wanted to do an observational study where people went on about their business. We had them give us information about what they were doing and we had them provide us with lots and lots of samples. So we had to figure out a fairly clever way to allow them to collect samples, to store the samples, and bring them back to us at refrigeration temperatures.

So we came across these portable thermoelectric coolers that could really contain a fair amount of samples as you will see. And we basically each -- each thermoelectric cooler represented a daily kit. And we would give instructions, and diaries, and checklists, have everything color coded and bar coded, and make sure that the subject had everything they needed in that cooler. And they could plug it into the car or plug it into the wall and make sure all the sample stayed cool at all times.

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DR. SOBUS: So one of the really clever things that we did, I think, was we put these very inexpensive, very small temperature loggers that plug into the USB drive of the computer, and we put these in each of the kits. And that allowed us to do three things.

Number one, it allowed us to track cooler performance. So if we had -- some coolers just ran colder than others. And obviously, you want to keep samples, particularly biological samples as cool as possible. So if we had a sampling container that wasn't functioning well, we could easily track that and move it out of the rotation and bring in something else.

Second, as we start to get our pyrethroid data back in, it will be very interesting to look at the temperature data and compare it to the residues to make sure we didn't have -- or we have no evidence of degradation.

Because this study went over, you know, several seasons, the coolers perform a little bit differently in a winter month, as they would compared to a summer month, because they bring the temperature down so much below ambient. So that's definitely a consideration.

And then the third point is monitoring subject compliance. No matter how often we told subjects to take the coolers home and to plug them in and keep them plugged in, they would always go home, put it in the corner, and not plug it until they collected their first sample. And when they'd come back to the clinic and we would plug this in, we'd say, "You didn't follow directions and we can see that".

So it was a great way to have reinforcement to make sure the subjects were following directions. And they kind of had an aha moment of oh you are watching me.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: Five more minutes.

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DR. SOBUS: Yep. So I'll cruise through these last slides. These are just some pictures of what the human studies facility work looked like. We had to assemble hundreds of these kits, but we did it very successfully. We would store all the kits in groups. Each subject would take two coolers with them for the beginning of the week and then two coolers with them for the end of the week. We never had any complaints about that being too cumbersome.

We did -- two of us would handle the training sessions, about an hour and a half per subject, and we would walk them through the daily coolers. And then when subjects would come back in -- I think this was another really clever thing we did. Again, we're getting full volumes of literally thousands of urine samples, and we have to get an accurate estimation of the volume. The last thing you want to do is to be doing graduated cylinder measurements of those of urine samples for various reasons.

(Laughter.)

DR. SOBUS: So when I was told that I would probably be doing that as we were checking in the subjects, I came up with this little thing that I named the Sobusizer, which was plastic sleeve that we put etchings on with different volumes. And we could just slide it over the sampling container, read off the measurements. We did some experiments. This had great precision, great accuracy. It worked phenomenally well.

So for anybody doing -- again, I'm a huge advocate of getting the full sample, getting the time of the void, and this is a fantastic way to very quickly and accurately and cleanly get the volume.

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DR. SOBUS: Again, I'm just going to fly through these. In addition to the trainings, we gave beautiful instruction manuals to the subjects that they were located in the corner pockets of these coolers. We would tell them every day before you go bed read the instructions for the next day, because we don't want you waking up, doing your first morning void, and then looking at your instructions and saying,"Ah, I was supposed to get that".

So we gave them very clear directions, showed them how to fill out the diaries, showed them how to collect their samples, made sure that they filled out the

time of the samples and the corresponding time on the activity diaries.

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DR. SOBUS: This is an important point. Everyone I've talked to -- not everyone, but most of the people I've talked to, including NHANES, uses 500 ml containers for doing urine sampling. We tested that and it wasn't enough. So we used one liter containers. And I'll show you some statistics in a minute, but we could fit 11 one liter containers in these thermal electric coolers in addition to the duplicate food samples.

So these things had great capacity, but it's just like carrying around a piece of luggage. So this really did work fantastically.

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DR. SOBUS: This is just a quick example of the checklist that we'd have subjects check off at the end of every day to make sure that they didn't miss anything.

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DR. SOBUS: I wanted to give some statistics on how successful we were. There was a total of about 4,000 samples that could have been collected. We calculated about 2,600 events that actually happened during the collection periods. We had a 97 percent completion rate in terms of getting the samples. Only three percent were

acknowledged missing. We had very, very few partial voids, which is a little bit unbelievable. And because that's so unbelievable, I said I need to go make sure that this is truth. So I came up with a little basically five-step methodology for evaluating if a subject was lying to us about missing a sample or having a partial void.

Because if they missed a sample or had a partial void, it's a big deal. You're going to underestimate the day's urine output, you're going to underestimate the day's chemical excretion and ultimately you're going to underestimate exposure. And that's not something we want to do.

So the visual is a lot more easy than the statistics.

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DR. SOBUS: There's a statistical component of this that I did. But you can see here we had a subject that was -- these were all 24-hour periods. There's six of them. You can see there were clearly between 1 and 10 ml per minute across the board. And they had this one observation that was just way out, close to 0.1 ml per minute. I confirmed it as an outlier with a normal probability plot. Again, I did some statistical evaluations and I looked at creatinine specific gravity.

And through that, I only found about 17 samples that I believed to be suspicious.

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DR. SOBUS: This is just for your reference. Again, like I said, 500 ml container, we would have lost somewhere above, I don't know, the 85th percentile. We had lots of people -- or lots of samples, I should say, that produced samples in excess of 500 ml. So if you use a 500 ml container, again you're going to underestimate urine output and ultimately underestimate exposure.

So that's something to consider if you're doing full voids, which again I'm a huge advocate for. And this is just to give you an idea of the range of void events over a day or a 24-hour period. We had an average of about seven to eight, but as few as three and as many as 14. So there's certainly some planning. But again, our coolers allowed as many as 11 in a particular 24-hour period, so we had very little loss of sample due to an extreme number of events.

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DR. SOBUS: So we had some really good keys to success. Again, the training sessions went extremely well. We would give subjects these ad hoc refreshers as needed, especially when they came back for week six sampling. The instruction manuals were absolutely a huge

hit.

Let's see. You know, QA check points everywhere. We're trying to get more into the technology benefits and allowing that to really enhance our studies. So where we put bar codes on everything and did direct data uploads and did temperature loggers, I think going forward we're really going to try and implement some of these technologies. And I would really recommend them for others.

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DR. SOBUS: Electronic diaries rather than hard copy diaries, especially with reminder alarms, because we saw many incidents where subjects would come in with an empty diary. And you'd see that look of panic on their face, and they would say, "Oh, darn it. I'm going to go fill out my diary".

So I think to the extent that we can use tablet and smart phones and have reminder alarms for electronic diaries, that would be huge. Using smart phones to do bar code scans for consumer products and the sampling containers would be extremely efficient, and ultimately taking advantage of web applications for, you know, meal snaps, seeing how many calories are in a meal, you know, how much activity, how many miles walked per day, that kind of thing, would be really, really advantageous.

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DR. SOBUS: And just to drive some things home. I hope I've helped convince people that there's really cool innovative ways to go about examining existing data and collecting new data as we go forward. And I think the collecting new data thing, as I heard earlier today, is going to be really, really interesting. And I think we really want to participate in some of this untargeted analysis, because there's many, many chemicals that we're not considering as biomarkers right now, and we really have to do evaluations on thousands of chemicals.

So to be thinking about how we can enhance biomonitoring to be evaluating models that make predictions with respect to exposure and toxicity for lists of thousands of chemicals, that will become really, really critical.

So thank you so much for your attention. I hope this resonates with some people and hopefully it will be meaningful and the start of further discussion.

Thank you.

(Applause.)

ACTING CHAIRPERSON BRADMAN: So thank you, Dr. Sobus, for that very interesting presentation. Definitely relevant to the work of the Biomonitoring Program and many others of us who are collecting these kind of

measurements. So we have some time right now for Panel questions, and that will be followed by opportunities for public comment. So if there are any thoughts and questions among the Panel?

Dr. Quintana.

PANEL MEMBER QUINTANA: Hi. Thank you for that whirlwind tour. I had some comments and I don't want things to sound negative, because I realize if I start -- it's not like I'm criticizing everything you're doing, I'm not. But I had two comments. One was on the biomonitoring equivalents. And I thought you were going to show that graph with the hazard index and the ranges that was in one of the materials you submitted. And this is where you are picking the amount of biological contaminant in the body that would correspond to the regulatory levels, is that correct?

DR. SOBUS: I'm not sure if you're referring to something I submitted or something that was submitted by Summit Toxicology.

PANEL MEMBER QUINTANA: Or something that was submitted -- a public comment, sorry.

DR. SOBUS: Right.

PANEL MEMBER QUINTANA: But didn't you -- but you're not involved in generating the biomonitoring equivalents, just in critiquing them, is that what you're

saying?

DR. SOBUS: I don't know if I'd say critiquing them. Perhaps thinking of innovative ways to help enhance them -- or help enhance the interpretation against them.

PANEL MEMBER QUINTANA: Okay.

ACTING CHAIRPERSON BRADMAN: I think you're referring to slide 16, where he talked about kind of a theoretical biomonitoring equivalent as a cutoff to evaluate. And I think that was just used as a simulation.

DR. SOBUS: Correct.

ACTING CHAIRPERSON BRADMAN: That wasn't an actual biomonitoring equivalent.

PANEL MEMBER QUINTANA: No, I agree. I guess my -- I have two comments on that slide going back to slide 16, which was the -- you said what percent of the population would exceed a value. And if you had a very stable biomarker, you're saying a single measurement would be more accurate than if it was -- it had variability, then you have fewer exceedances. But I think this is true given your assumption that it's the long-term exposure that matters, but I --

DR. SOBUS: Correct.

PANEL MEMBER QUINTANA: -- do want to say, there are many situations, and pregnancy is one, where -- and I'm thinking specifically of the atrazine controversy in

the water, where they -- I believe they were averaging the level of atrazine to compare to a standard, but in fact there were these events with very high atrazine concentrations. And so -- and if you were pregnant and you drank the water that day, that might have a significant effect on your baby. And it was really related to peak events and not the average level of atrazine.

DR. SOBUS: Absolutely.

PANEL MEMBER QUINTANA: And so I just think if you make these models, it's important to emphasize what the underlying assumptions are --

DR. SOBUS: Right. And at this point --

PANEL MEMBER QUINTANA: -- which may not be appropriate for some outpoints.

DR. SOBUS: I think I made the point today that, you know, this is really looking at where risk is being evaluated based on long-term term exposure. And we certainly make a point of that in the paper, but that's an absolutely excellent point.

PANEL MEMBER QUINTANA: And I also think that the idea of biomonitoring equivalents is really useful, but I think getting back to Dr. Quint's comment earlier about the OSHA PEL for chromium, where people might start taking standards as meaning it's okay, as opposed to this is a

number that was come up with with a huge amount of controversy. For example, arsenic in drinking water, some people wanted it lower, you know, some higher. And so that level might be used as a hazard index, but it was not necessarily the health-based level.

DR. SOBUS: Sure. We actually have a discussion of that in the paper too, in that one of the reasons that we kind of artificially chose a biomonitoring equivalent level is that you can pick any level of interest.

The goal here is to say we've been limited, in that when you compare a distribution of spots to a BE, you're basically using only the median value, and you're not really focusing on the upper percentile of the distribution, or, if you are, you're kind of -- you're lacking confidence in what that means. So this is a mechanism to make it an apples to apples comparison.

The value you choose for the BE is up to you, so if you don't want to take into account uncertainty factors, or if you want to use a PEL instead, I mean, that's all completely appropriate. It's the mathematics of going from the distribution of spots to a distribution of averages, and then interpreting that based on average exposures. And again, if you're talking about peak events being related to toxicity, this isn't the method for you, but I mean your points are absolutely on point.

PANEL MEMBER QUINTANA: And the last -- very last comment -- sorry -- is that when you started out, you're talking about interpreting your N values, for example. And you had daily intake in your model for phthalates, for example --

DR. SOBUS: Right.

PANEL MEMBER QUINTANA: -- but there's behavior variability that goes into that as well. For example, cotinine has a short half-life, but it's a pretty accurate marker of cigarette smoke exposure, because the behavior is so stable. Whereas, something else with a short half-life that you're only exposed to once a week at the gas station might be more variable, but those two situations might look the same in your model, because you're just looking at a certain -- you know, you're not looking at the behavior variability on top of the other stuff as well, I guess.

DR. SOBUS: So I'm not sure, are we talking about the risk-based or --

PANEL MEMBER QUINTANA: I can't remember.

DR. SOBUS: -- or the association-based approaches?

PANEL MEMBER QUINTANA: I'm talking about the slide -- you showed a lot of slides. Way down to slide -- the very beginning of your talk. I can't see without my

glasses. I'm just saying is that there's a lot of things that go into making up variability, which can't always be captured with just starting with a PBPK model on a daily intake.

DR. SOBUS: Oh, absolutely. And that's why, again, I think -- I tried to separate the talk into existing data being so much of spot measurements, and having no idea how to understand variability with spot measurements to going forward in the studies that we're doing collecting lots and lots and lots of samples to understand variability and sources of the variability, be it going to the gas station or something else.

So that's why I said project one is we're using what we've got and we're trying to use it to the best of our ability. Project two is how do we be clever about going out and getting the information that we need. So I agree with you 100 percent.

PANEL MEMBER QUINTANA: Sorry for such a long comment.

ACTING CHAIRPERSON BRADMAN: Any other questions by the Panel for Dr. Sobus?

I have a question -- kind of a technical question going back to slide 16, and the points leading up to that. In terms of the -- you must -- to get an ICC, you have to have some repeat samples. And I'm curious, have you

looked at in terms of the length of time between the samples and how long that should be depending on the estimated half-life of the compound?

DR. SOBUS: We had -- our team had a tremendous amount of discussion about this, and absolutely, the length of time, the population of interest. What we found to be extremely important, and we describe in the paper I skipped over today, is the number of repeats that you have. You have a lot more confidence in your variance components in your ICC given that you have more repeated observations.

ACTING CHAIRPERSON BRADMAN: Exactly.

DR. SOBUS: And then we've also talked about if ICCs are collected or based on repeated measurements over a week, how does that pertain to a month, or a year, or ten years? So these are all fantastic questions.

So the goal with this paper was just to put out a methodology that says given that you know something about it, can you do it?

Now, what we're doing is going out and getting that data and doing it for more chemicals.

ACTING CHAIRPERSON BRADMAN: It doesn't look like we have anymore comments. I just want to reiterate that was a fascinating presentation and I think really addresses some of the kind of core issues in exposure

assessment and biomonitoring that face a lot of us these days, particularly for nonpersistent compounds, which are such a challenge. Urine is such an easy media to take measurements in, but how to use that is challenging, and it's great to see your group addressing those questions.

So I think that's it.

Thank you.

DR. SOBUS: Thank you so much.

ACTING CHAIRPERSON BRADMAN: At this point, we have some time for public comment related to this previous presentation session. And are there any public comments in the group here?

MS. DUNN: None.

ACTING CHAIRPERSON BRADMAN: No. Okay.

Then we have one comment that was submitted last night by Lesa Aylward from the Summit Toxicology Group. They've talked to us before, and I'm going to read some highlights from their letter, which is perhaps related to some of the early conversation. So this is -- again, this is from Sean Hays -- Dr. Hays and Dr. Aylward from Summit Toxicology.

"Dear distinguished Panelists...," with respect to interpretation to biomonitoring data, "...Since we, (Lesa Aylward specifically), presented to the Science Guidance Panel in March of 2011, we've made significant

progress in developing biomonitoring equivalents as a tool for interpreting human biomonitoring data. The biomonitoring equivalents allow interpretation of population-based biomonitoring levels and allows an assessment of the margins of safety and/or hazard quotients on a chemical-specific basis. Comparing MOSs, margins of safety, and/or hazard quotients across chemicals also allows a relative ranking that can serve as a very powerful tool to allow public health agencies to prioritize which chemicals pose the greatest threat to public health amongst the population.

"We encourage the Scientific Guidance Panel and the Biomonitoring California staff to utilize biomonitoring equivalents and/or other such approaches to interpreting biomonitoring data in a public health risk context. While the biomonitoring equivalent values are simply an initial screening tool, they do provide some initial insight into the question of, 'what do the measured biomarker levels mean?'"

I should mention there's a footnote here that, "The biomonitoring equivalent is defined as the concentration of a chemical, or metabolite, in blood or urine that is consistent with an established tolerable exposure guideline, such as reference dose, tolerable daily intake, et cetera."

And again, that was signed by Sean Hays and Lesa Aylward. And there's a little bit more length in here that I didn't take the time to read today, because we're constrained. But again, this comment is published on the Biomonitoring website. And there's also some related supporting information, including papers and other literature.

So we now have some time for Panel discussion related to this previous discussion, then we will have time for open comment on anything related to today and the Biomonitoring Program, and then we'll have a wrap-up and announcement.

So I know I have some comments with respect to this recent public comment. But I'm wondering if there's any other input or comments from the Panel on anything we've heard in the last presentation?

Dr. Fiehn.

PANEL MEMBER FIEHN: Okay. So I couldn't follow everything the presenter said, and -- but I wondered when you did your modelings, did I perceive this correctly that you said if you do the creatinine adjustments, you introduce bias? Is that, shortly, what I understood correctly, when I have to go home?

DR. SOBUS: Is this on? Can you hear me? Is this -- for that association-based study, that is not a

universal truth. What we were hoping to get from that simulation was basically a procedure for going about identifying bias.

So the result from that particular study, where we were looking at body mass index and waist circumference as the outcome variable, creatinine-introduced bias. And that is because creatinine excretion is a function of body size. So if a different outcome that was independent of creatinine were being considered, creatinine may be a very good tool for correcting for urine output.

So the goal of that wasn't to say this is good, this is bad, it was to say you need to think about it and this is how you should go about thinking about it. So we try and detail, you know, kind of guidance for -- not doing a full-blown simulation obviously in every example, but some steps you can take to try and identify which would be the best to use.

PANEL MEMBER FIEHN: That makes more sense.

ACTING CHAIRPERSON BRADMAN: But I think though -- I guess we're going to go back to your presentation, and a question. From slide 11, I think there was an implication there that the creatinine-adjusted value would be the least biased predictor, if, in fact, there was a relationship -- it would be the least biased exposure metric, if, in fact,

there was a relationship between the exposure and the outcome in this case.

DR. SOBUS: So I believe you're referring to this slide. So what I wanted to communicate with this slide was in the simulation results in that middle category where you see no effect --

ACTING CHAIRPERSON BRADMAN: Right.

DR. SOBUS: -- those would be the exposure surrogates that were not associated with bias.

ACTING CHAIRPERSON BRADMAN: Correct.

DR. SOBUS: And that is because the meta-data that went into producing concentration, and that value being urine output, and excretion rate, that being time between voids, are independent of body size. That's why we had no introduced bias in those associations. The negative effect says there was a significant negative association.

ACTING CHAIRPERSON BRADMAN: Right. I'm sorry. I misspoke. I meant the random -- yeah, the excretion rate.

DR. SOBUS: Okay.

ACTING CHAIRPERSON BRADMAN: So based on this -- on your simulation result, you would say that the excretion rate was probably the best -- the least biased predictor of the outcome in this analysis?

DR. SOBUS: Yeah. You know, me personally, my default would be excretion rate. It won't always be the best. But based on my observations, it's something that I would typically start with and then think about other things. I was -- I wasn't surprised to see the concentration had no bias. But for this analysis, concentration and excretion rate performed equally well.

ACTING CHAIRPERSON BRADMAN: All right. Okay. Thanks.

Well, I guess in terms of Panel discussion then I have one comment in response to the public comment and letter submitted by Summit Toxicology. First, I want to say I think the biomonitoring equivalent field and approach to evaluating measurements I think is very valuable. And I think it's a great contribution to the science and really gives us ways to think about how to interpret these results.

But we've talked about this before as a Panel, and, you know, as she recommended to us, we encouraged the SGP and the Biomonitoring California staff to utilize biomonitoring equivalents and/or other such approaches for interpreting biomonitoring data in a public health risk context.

In the past, we've had discussions on the Panel around that issue. And, in general, we, or at least I,

have felt strongly that the Biomonitoring Program should not get involved in risk assessment and risk evaluation. That because of the complexities and challenges of that, really the goals of the Program should be to produce good information on exposures and measurements in matrices. And that the risk interpretation, while important to do, should occur in some other context, so the Biomonitoring Program itself won't be bogged down in the debates and often political controversies that come over the risk assessments and risk management.

I just want to respond to that, but I still very much respect the work being done by Summit Toxicology on these issues.

Sure. Dr. Quintana.

PANEL MEMBER QUINTANA: Hi. Jenny Quintana.

Will, first of all, I guess I'll make the comment to Dr. Sobus that I got mixed up. It was -- this submitted document -- yeah, one of my comments was addressing was stuck to his presentation, and I thought -- I got mixed up it was his too. So that being said, I want to clarify that one of my comments wasn't addressed to him. But I do want to echo what you just said, that I think that the interpretation -- that this very interesting approach biological equivalents, but endorsing them as being safe or at the hazard level is beyond the

scope of this Committee. And I feel like, although I appreciate the work that's being done, I feel we should stick to providing the most accurate exposure data that we can, to endorse your comments.

ACTING CHAIRPERSON BRADMAN: So at this point, I think then we're actually getting back on time here. We now have a period for open public comment of up to 15 minutes.

MS. HOOVER: Actually, this is Sara Hoover of OEHHA. Before we move off, so the open public comment period is actually closing Dr. Sobus's item, and it's not related to Dr. Sobus.

So before we close off, I wanted to just open it to, you know, any staff -- Program staff or, you know, important Program advisors to just think about or comment on going forward are there ways that people envision, you know, continuing? I mean, we have -- I find Dr. Sobus to be really interesting in what he's doing, a great opportunity for the Program to work with EPA. So more comments about, you know, what are intersections between the kinds of things he's doing and our Program? Any thoughts at all in that regard before we move off into the open public comment? So anybody at all in the Program or on the Panel thinking in those terms?

ACTING CHAIRPERSON BRADMAN: Dr. Fenster.

DR. FENSTER: Hi. I really enjoyed the presentation. And I found myself also feeling like a field epidemiologist, in that work that say CHAMACOS has done, literally collecting samples in the field where it's difficult to even get samples back to a lab in terms of assuring quality control, you know, makes me feel like the work that EPA is doing is particularly of interest to find ways where we can extrapolate from those more ideal data collection methods to other ways we can collect data from a very disparate population in California, because I think that's really, to me, where the -- you know, the value in the future and continued discussion, in terms of us being able to extrapolate lessons from more of an ideal collection with a particular group of people that you have been able to use to collect data, in terms of the second piece of your -- of your presentation. Because I think that, you know, it's a very rare and it's very great data collection methods. And if we can extrapolate and ways we can be more efficient in collecting our data, that would be a great collaboration.

DR. SOBUS: This is Jon Sobus again. I wanted to make one other point that -- I know I covered a lot of material very quickly, but one of the things I didn't have a chance to get into is something that we talked about earlier today and that's -- you know, we covered uses of

existing data, and collection of new samples.

What we're really thinking about now is doing this kind of untargeted analysis. And at the Agency, particularly in the Chemical Safety for Sustainability Research Program, we have the charge of prioritizing very large lists of chemicals based on anticipated exposure, hazard, and ultimately risk.

So we've been developing models and different testing techniques for trying to make predictions on a very large number of chemicals. And ultimately to evaluate that, we think biomarkers will be a terrific tool and measurements in general. So we're really starting to think about and apply some methods for doing some of these untargeted type measurements.

So I'd like to put out there that -- so we don't reinvent the wheel, that if groups are being formed here in the State, we would love to be part of that discussion to think about, you know, the different analytical platforms that are being used, the different media that are being measured, and to think about what EPA could contribute, so that again we're not reinventing the wheel, that we have a particular niche, and hopefully, it would be a very nice relationship to start.

ACTING CHAIRPERSON BRADMAN: Dr. Quint.

PANEL MEMBER QUINT: Julia Quint.

Yeah, I really enjoyed reading your papers and enjoyed the talk. And I think, for me, since joining the Panel, what's most important here, what we're all trying to get at is reduction of exposure. And, you know, risk aside, we really want to reduce the hazards. So I think the -- if there are ways to collaborate on how when you're -- we're doing these studies to collect better exposure information would be really, really helpful, because often we can come up with levels in bodies, but then trying to figure out where those chemicals came from is the real challenge.

And so -- and I think your papers are the first that I've seen that really sort of honed in on that whole exposure relationship to bio -- I mean, I'm sure others have -- but to put it so clearly. You know, there are occupational studies where you have very good information about exposures. And we've had biological exposure indices in occupational health for a long time, but it's gone nowhere in terms of reducing hazards, as far as I'm concerned, because the standards are -- the PELs are still -- you know, have a lot of risk attached to them. So we've not used it in terms of chronic toxicity the way we should have.

So anything that we can get at in terms of collecting better exposure information, better

questionnaires, however we do that, would be tremendously helpful to this Program. And collaborations on that level would be wonderful.

ACTING CHAIRPERSON BRADMAN: I'll make one last offer.

I'm sorry. Dr. Zeise.

DR. ZEISE: Just one more point with respect to the collaboration. It would be absolutely wonderful to work more with you, and -- Lauren Zeise with OEHHA.

And one of the big issues with the non-targeted sampling that's been particularly difficult is figuring out the metabolites and coming up with a reference list for metabolites, and I think making some progress in that area. I don't know what you all are doing in that regard, but we're finding it particularly difficult. So I don't know if you want to comment on that.

DR. SOBUS: Just to respond to it. Jon Sobus. To the best of my knowledge, it's something we've been talking about too. I don't believe we've made any headway. I would say we're fairly new to the field of trying to get into untargeted work, but that whole metabolism issue is something that has come up, and there's been discussions at the high management level about it.

So it's something that we're taking into

consideration as we plan for how we're going to do this work, and as we try and align instrumentation, and again think about chemicals and samples to look at, and figure out just the best strategies going forward. So again, you know, I think we're probably having a lot of the same discussions internally, but I think it will be very fruitful to have those discussions in a larger group.

ACTING CHAIRPERSON BRADMAN: Just one last comment or perhaps an opportunity for collaboration. We have a set of samples collected from three to six year olds spot and 24-hour samples collected over a week period. And we've been wanting to conduct or complete a collaboration with this Biomonitoring Program to look at phenols and phthalates and other metabolites in those samples to get at issues around, within, and between variability.

We published one paper on pesticide metabolites, but there's a lot more that can be done with that. And that's perhaps something that we could move forward on perhaps try to get resources to measure them and to do the whole set. So there might be an opportunity here to perhaps address some of the questions that you're interested in and also the Program here.

So again, we're right on time actually now at 4:20 to close the previous discussion around the

presentation. And we now have a open public comment period. And then after that, we'll have a wrap-up and adjournment. It looks like we do have a public comment from Nancy Buermeyer.

MS. BUERMEYER: Buermeyer.

ACTING CHAIRPERSON BRADMAN: Buermeyer -- thank you -- from the Breast Cancer Fund.

MS. BUERMEYER: Thank you very much. And I know we're -- it's late in the day, so I'll try to be brief. And I just wanted to take a minute to thank the Panel for all the work that you do to support this Program and clearly the homework you do before you get here, and your comments here. And to thank the staff of the Biomonitoring Program, which I know works tirelessly day and night putting all these materials together, and creating a world-class Program that we in California are extremely, extremely proud of.

We've geeked out a little bit today talking about metal speciation and validated methodologies and intraclass correlation coefficients, which as an advocate I have no idea what that is --

(Laughter.)

MS. BUERMEYER: -- but you sounded really smart explaining it, Dr. Sobus, so thank you.

(Laughter.)

MS. BUERMEYER: And I just wanted to sort of take a step back to let you know that this Program is really valuable -- is really valuable to folks outside this room.

The Breast Cancer Fund organized a letter to the Governor asking for State funding for this Program, given the challenges you'll have with the loss of at least some of the CDC funds.

So we organized a sign-on letter to the Governor. And I just wanted to take one minute to read you the list of organizations that signed this letter and support this Program really strongly:

The Breast Cancer Fund, surprisingly, California Healthy Nail Collaborative, California National Organization for Women, Center for Environmental Health, Clean Water Action, Coalition for Clean Air -- and please excuse my Spanish on this -- Comite civico del Valle, Commonweal Biomonitoring Research Center -- Davis in absentia -- the Environmental Working Group, Friends of the Earth, Natural Resources Defense Council, Pesticide Action Network, Physicians for Social Responsibility Los Angeles, San Francisco Bay Area Physicians for Social Responsibility, and the United Fire Service Women, which is an organization of women firefighters in San Francisco.

And I'm sure there are lots more organizations that are out there that would have signed this had they

had time and I had time to track them down. But I just want you to know that what you do is really appreciated out in the world by the communities that are impacted by these chemical exposures, and to say thank you from all of them for the work that you do and for the work that the Panel does in supporting this Program.

Thank you.

ACTING CHAIRPERSON BRADMAN: Well, I think then we are approaching the end of today's meeting and now, time for a wrap-up and adjournment.

I want to announce that a transcript of this meeting will be posted on the Biomonitoring California website when available.

Also, a reminder that the next meeting of our group will be on July 10th also in Oakland, and also to let you know that the conference facility here will close promptly at 5:00 and that we recommend heading down to the lobby as soon as we're done.

(Laughter.)

ACTING CHAIRPERSON BRADMAN: So if you need to schmooze, we'll have a little time up here, but you should schmooze down in the lobby downstairs.

And I think Dr. Alexeeff, do you -- are you going to provide a wrap up for today's meeting?

DIRECTOR ALEXEEFF: No. I was just going to say

we would be -- we will be posting the transcript on the website when that's done. And we did discuss designating and prioritizing chemicals today, and that's a lot of the hard work of the Panel. We had a great presentation from Dr. Sobus, and also updates of the laboratory and the other staff work that's going on.

I want to thank the Panel for again taking time out of their busy schedule to come here to advise the State on this very important Program and giving us direction, and utilizing the resources that we have in this Program wisely, in helping us to collaborate with other agencies, universities, and departments in the State.

So thank you very much.

ACTING CHAIRPERSON BRADMAN: I think we're officially done.

Thank you.

(Thereupon the California Environmental Contaminant Biomonitoring Program, Scientific Guidance Panel meeting adjourned at 4:24 p.m.)

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

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

That I am a disinterested person herein; that the foregoing California Environmental Contamination Biomonitoring Program Scientific Guidance Panel meeting 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 meeting nor in any way interested in the outcome of said meeting.

IN WITNESS WHEREOF, I have hereunto set my hand this 10th day of April, 2014.

JAMES F. PETERS, CSR, RPR
Certified Shorthand Reporter
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