MEETING

STATE OF CALIFORNIA

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

ENVIRONMENTAL CONTAMINANT BIOMONITORING PROGRAM

SCIENTIFIC GUIDANCE PANEL

CAL/EPA HEADQUARTERS BUILDING

COASTAL HEARING ROOM

1001 I STREET

SACRAMENTO, CALIFORNIA

THURSDAY, JULY 14, 2011

10:09 A.M.

JAMES F. PETERS, CSR, RPR
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APPEARANCES

PANEL MEMBERS

Ulrike Luderer, Chairperson, M.D., Ph.D.

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

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

Thomas McKone, Ph.D.

Julia Quint, Ph.D.

Gina Solomon, M.D., M.P.H.

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

Dr. George Alexeeff, Acting Director

Ms. Carol Monahan-Cummings, Chief Counsel

Mr. Allan Hirsch, Chief Deputy Director

Ms. Amy Dunn, Safer Alternative Assessment and Biomonitoring Section

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

Dr. Gail Krowech, Staff Toxicologist, Safer Alternatives Assessment and Biomonitoring Section

Dr. Lauren Zeise, Chief, Reproductive and Cancer Hazard Assessment Branch

DEPARTMENT OF PUBLIC HEALTH

Dr. Rupali Das, Chief, Exposure Assessment Section, Environmental Health Investigations Branch

Dr. Jianwen She, Chief, Biochemistry Section

APPEARANCES CONTINUED

DEPARTMENT OF TOXIC SUBSTANCES CONTROL

Dr. Myrto Petreas, Chief, Environmental Chemistry Branch

ALSO PRESENT

Mr. Davis Baltz, Commonweal

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PROCEEDINGS

OEHHA ACTING DIRECTOR ALEXEEFF: Good morning, everyone. We'll go ahead and call our meeting to order.

I'm George Alexeeff, Acting Director of the Office of Environmental Health Hazard assessment. And I want to welcome the Panel. And I believe we have one more Panel member coming. I want to welcome the public both present here as well as on line.

And also the staff, I want to thank the staff for all their hard work they did in preparing this meeting, and for attending it hear to answer questions.

And this is the meeting of the Scientific Guidance Panel for the California Environmental Biomonitoring Program -- Contaminant -- there we go -- for the California Environmental Contaminant Biomonitoring Program, also known as Biomonitoring California, and that's why we also know it as Biomonitoring California, it's pronounceable.

So I want to thank, again, the Panel and the public for taking time out of their busy schedules to attend this meeting and to provide advice to the State regarding the Biomonitoring Program.

And I need to make a couple of announcements with regards to the logistics. First of all, restrooms. They're out the back and to the left. And then in the

event of a requirement of an evacuation, you'll need to leave the room, take your valuables, go out the back or the side entrance, or we'll go out this entrance, go down the stairs, and then the evacuation point is the park across the street.

So I wanted to remind everyone that this meeting is being webcast, and it's being recorded, and it's being transcribed. There will be a transcript of the meeting posted on the website in several weeks. And since there are people listening via webcast, please be sure to speak clearly into the mic.

So I'll just briefly give an overview of the last meeting of the Scientific Guidance Panel. That was held in Oakland on March 16th. At that meeting, the Panel provided suggestions for improving a chemical selections screening tool to help identify candidates for potential designation.

The Panel responded to questions on quote, "Looking forward for Biomonitoring California", to aid with the program planning. The Panel provided input and recommendations on the other agenda topics, which included program and laboratory updates, biomonitoring literacy, developing report-back materials with input from the study participants, and the Kaiser Permanente collaboration Biomonitoring Exposure Study, also known as BEST.

For a summary of the Panel's recommendations, and input at the March meeting, you can see all the information at the -- on the website at biomonitoring.ca.gov.

So I'd like to now turn the meeting over to Dr. Luderer.

CHAIRPERSON LUDERER: Thank you, Dr. Alexeeff. I'd also like to welcome everyone, members of the public listening via webcast, and also here at the meeting, the California -- Biomonitoring California staff and the Panel members.

And I wanted to just briefly summarize what the goals are for the Panel for the meeting today. So the Panel will receive program and laboratory updates and provide input to the program. We will hear an update on chemical selection activities and provide input on the revised screening approach for possible candidates for designation, which will be illustrated using an example of organotins.

We'll hear a presentation on non-targeted screening of biological samples for environmental contaminants, and provide recommendations. We will also discuss the March 17th, 2011 workshop on understanding and interpreting biomonitoring results and provide recommendations. And we'll discuss preparing a letter

with Panel recommendations for the Program to be included in the upcoming 2012 report to the Legislature.

I just wanted to remind everyone also that each presentation will be followed by an opportunity for Panel discussions, as well as a public comment period and then time for further Panel discussion and recommendations.

If any member of the public would like to make a comment, then he or she should fill out a comment card, which can be obtained from the staff table outside the room --

MS. HOOVER: Actually, in the back of the room.

CHAIRPERSON LUDERER: In the back of the room, okay. And please turn them into Amy Dunn. Amy, could you identify yourself, please.

MS. HOOVER: She's actually out of the room right now, so she'll be sitting up here.

CHAIRPERSON LUDERER: Okay. Great.

And then members of the public who are not here, but are participating via the webcast and would like to submit comments can send an Email to the Biomonitoring Email address, which is biomonitoring one word at OEHHA, O-e-h-h-a, .ca.gov during the meeting. And Biomonitoring California staff will provide the comments to me so that I can read them allowed at the appropriate time.

To make sure that the meeting proceeds on

schedule and that every commentator has the opportunity to speak, the comments will be timed and will be subject to time limits. So we'll basically divide the time allotted for public comments equally among all the individuals wishing to speak.

So please also remember to keep your comments focused on agenda topics being presented. And then at the end of the day, there will also be an open public comment period.

I also wanted to again remind everyone to speak directly into the microphone and please introduce yourself before speaking. And this is for the benefit of the people participating via webcast, as well as for the benefit of the transcriber.

So the meeting -- the materials for this meeting are provided in a meeting folder for the Scientific Guidance Panel members and via the website for the public. And there are also a small number of handouts and one folder for viewing at the staff table outside the auditorium.

I also wanted to mention that we'll take two breaks today. The first one will be for lunch around noon, and then there will be a break in the middle of the afternoon sessions.

Now, that we've taken care of business, I wanted

to announce the first item on the agenda is an update on the California Environmental Contaminant Biomonitoring Program activities. And Dr. Rupali Das who is Chief of the Exposure Assessment Section, California Department of Public Health and lead of Biomonitoring California will make that presentation.

Dr. Das.

(Thereupon an overhead presentation was presented as follows.)

DR. DAS: Thank you, Dr. Luderer. Welcome to the members of the Scientific Guidance Panel, audience members who are attending here in the auditorium as well as those of you attending via webcast.

Pardon me, while I get to the beginning of the presentation here.

As Dr. Luderer announced, it's my pleasure this morning to provide you an update of the overall program for the California Environmental Contaminant Biomonitoring Program, also known as Biomonitoring California.

I want to thank all the staff who work on this program that are not acknowledged at the end, but are actually too many to list in their entirety. And also thank the staff who helped put this presentation together.

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DR. DAS: You see here an outline of my

presentation. I'll be providing the usual updates on the funding status, staffing changes, describe the progress we've made on the three pilot projects, describing briefly an update on the public involvement plan, our activities to proceed with strategic planning for the Program as a whole and a few other items that we've been engaging in.

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DR. DAS: Our funding as you know, comes from two sources. State funds come from the Department of Toxic Substances Control specifically to support Biomonitoring California. And that is the Toxic Substances Control Account, or TSCA, which provides $1.9 million annually to fund staff from the three departments.

In addition, we have a five-year CDC cooperative agreement. We're currently in Year Two. Our fiscal year ends August 31st, and we will begin Year Three in September.

As I announced at the last Panel meeting, our year two funding remains stable at $2.6 million. And we submitted our application for the year three funds in the spring, and we're hoping to hear very soon about the status of the submission, as well as the level of funding, which we, at this point, expect to remain stable.

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DR. DAS: At the last meeting, I had announced

that we were in the process of hiring an administrative assistant. She started shortly after that meeting. Nancy Lopez is not able to be here in the room with us, but she's been a great addition to the Program, and I wanted to welcome her formally to the Program.

We also have some vacancies, three vacancies, across the program, two research scientists, and one research scientist supervisor. Two of these vacancies are due to retirements. One of the retirements is Diana Lee, who you know retired at the end of last year. She was instrumental in building many aspects of the Program. And the other is Dr. Frank Barley, whose retirement was announced by Dr. She at the previous meeting.

We're in the process of recruiting for both of these positions. We were also fortunate to have additional assistance in the Program. We had a Fogarty Scholar. Our Fogarty program is a collaboration with the Shanghai CDC. It's been ongoing for 10 years. The Fogarty Scholar did some considerable and innovative work in helping to develop methods to analyze infant blood spots. Unfortunately, the Fogarty scholarship period is only six months, and we regret that he had to leave, but he did some interesting work and Dr. She may speak a little bit more about that in his presentation.

We're also fortunate to have nine summer interns,

two in OEHHA, funded by State funds, and seven in the Environmental Health Lab funded by the CDC. And Dr. She will also introduce some of those interns who are here with us in the room today.

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DR. DAS: I'd next like to provide you an update on our three pilot projects. First, the Maternal and Infant Environmental Exposure Project, MIEEP, also known as the Chemicals In Our Bodies Project.

As you know, this was the first pilot project that we began actively collecting samples.

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DR. DAS: And we're happy to report that we have completed enrollment. Our initial intended target was -- we thought we were going to get 50 to 75 participants based on the funding. But with additional funding, we were able to recruit 92 participants, which we're very happy about. This is just shy of the ideal 100 that we were hoping for. But still, given the amount of effort that it takes to recruit women in their third trimester and then obtain biological samples during the labor and delivery, we're very happy that we got 92 participants.

So enrollment completed means that we recruited participants. They've delivered. We obtained the biological samples, which are urine, whole blood, and

serum. And the questionnaire completion -- questionnaires have been completed.

There are two questionnaires. The interviewer administered questionnaire, which was administered in the clinic and the self-administered questionnaire, which participants completed at home.

Dr. Tracey Woodruff, who is the PI at UCSF will be presenting more details about this project and its status at the November Panel meeting. I'll just give you a brief overview of our progress so far. We're happy to report that the analysis of blood metals has been completed for the mothers and the cord blood samples.

Unfortunately, whole blood and serum was not collected for all the mothers. And this was primarily due to the fact that some of the deliveries took place, either on weekends or at night when project staff are not available to remind clinical staff to collect some of the samples. And so while we obtained urine on just about all the mothers in the project, whole blood and serum was not collected for all mothers.

And cord blood was collected for fewer infants than mothers. And this was primarily due to difficulties in collecting the cord blood. But the process of collecting the cord blood was that it was collected in a beaker and then transferred to specimen containers. Where

we had to make a choice where there wasn't enough cord blood to provide both whole blood and serum samples, we prioritized serum, because of the analytes that we were primarily interested in.

So we have a few more serum samples for cord blood than whole blood. As I mentioned, we'll provide more details on the numbers in November.

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DR. DAS: Even though we've completed a big part of the MIEEP effort recruitment and sample collection, there's a lot of work left for us to do in the next coming months. We're completing the analyses for the biological samples. So other than metals, we have a lot more analyses to complete. We're entering and analyzing questionnaire data.

And a big push is going to go towards doing all the work that's involved in returning results back to individuals. At the last Panel meeting, you heard from Dr. Rachel Morello-Frosch and Holly Brown Williams about the template and some of the materials that they developed that we'll be using as a basis to return results. We still have to develop chemical-specific materials for the various chemical categories that we're analyzing. And a lot of work remains to finalize those materials. We're doing that in collaboration with Dr. Morello-Frosch at UC

Berkeley, as well as with UCSF.

After we return results to individuals, we'll be publicly disseminating the findings. And that includes presentations to this Panel, presentations at other scientific conferences, and peer reviewed publications.

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DR. DAS: One of the public health successes of biomonitoring in this project was the identification of an elevated mercury level. We detected an elevated mercury level in one mother infant pair. The level in the mother was twice the level that triggers early notification, which is 5.8 micrograms per liter and is based on the level set by the Centers for Disease Control and Prevention for pregnant women.

We conducted a follow-up investigation with UCSF staff, the county health department, and U.S. EPA. And in the process of that investigation identified the source of the elevated mercury as a face cream that was adulterated in Mexico and imported in hand luggage.

We issued a health alert to the local clinics and to the health department that had been developed last year in response to another incident investigation that we had conducted, when we identified an elevated mercury level in a number of families in the Bay Area.

As a result of this incident, we're considering

additional follow-up actions, including broadening our outreach and notification and possibly additional regulatory actions. This is a successful public health activity, because we identified an elevated case, we identified the source of exposure, and we worked with local, State, and federal departments and agencies, and expanded the number of agencies we were able to work with, even from our efforts last year. So I hope that this will lead to even more outreach and prevention, in terms of controlling mercury face creams as a source of exposure.

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DR. DAS: This is the health alert that was developed in response to the mercury investigation that we did in 2010. There's Spanish and English versions.

In addition to this health alert, which was distributed to clinics, Poison Control Centers in the U.S. as well as in Mexico last year, we also developed a public service announcement in Spanish that was broadcast on Spanish language radio in certain areas in California. And we're hoping that we'll expand this outreach as a result of this investigation.

The materials are accessible on that website that's listed at the bottom of this slide.

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DR. DAS: I'd next like to turn to our

Firefighter Occupational Exposures project, or FOX.

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DR. DAS: At the last meeting, I told you that we had completed recruitment of 101 firefighters. And at this point, I'm happy to report that we've completed the analyses for blood metals and the perfluorinated chemicals.

If you'll recall, we had also started dust sample collection with a separate pot of funds, not related biomonitoring. At that time, we had conducted dust sampling from five fire houses. Since the last meeting, we've expanded the dust sample collection to 20 fire stations. And our environmental chemistry lab, Dr. Myrto Petreas' lab, will be analyzing the samples for PBDEs, PCBs, and PAHs.

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DR. DAS: As with MIEEP, we have a lot of work left to do on FOX. We're completing the biological sample analyses, analyzing questionnaire data, and we'll be conducting usability testing specifically for FOX. So Dr. Morello-Frosch made a presentation on usability testing among mothers that was relevant to the MIEEP study. We feel that usability testing this population, firefighters, is really essential, because we want to use the template that Dr. Morello-Frosch developed, but improve on it and

make it specific to this population.

We feel that this population is different from the mothers. They're demographically different. They're different in education. They're workers. They have a different mentality about the nature of biomonitoring and many other things. And so we want to make the materials relevant to this population. I'll be mentioning a little bit more about this in the next slide.

We will be reporting results not only to the participants, but also aggregate results to the Orange County Fire Authority Oversight Committee that made our collaboration possible. This is a union-management collaborative committee, and we want to make sure they get the results -- the aggregate results around the same time that we return individual results. Following that, we'll be disseminating the results publicly as we plan to do for MIEEP.

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DR. DAS: Usability testing for the FOX materials will start next month. Currently, our documents are undergoing IRB review. And this will include the template for returning results and for several different chemicals. We've used the template developed by Dr. Morello-Frosch and have made some changes to improve on the language, as well as the graphic representation. And after we get some

results from the firefighters, I hope that we can present those results to you.

The firefighters that will participate in the usability testing are Orange County firefighters, but they're not FOX participants. They will also be drawn from the Wellness and Fitness clinic, but they are not the same participants that were biomonitored in the FOX study.

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DR. DAS: We learned a number of different things from the FOX experience, and we hope to use these lessons in future projects, and present some of them to you.

These are lessons that we compiled based on conversations with the clinic staff and with Dr. Israel, the PI and clinic director at UC Irvine.

Firefighters are busy. They don't want to spend a lot of time in the clinic, beyond what they have to do. They didn't -- we knew from the outset that they did not want to spend a long time filling out the questionnaire, and that's why we made the questionnaire no longer than 15 minutes.

However, the consent form was itself very long. And it was long, because it has a number of different components that are required to be in there due to federal requirements. We learned that participants didn't really want to read the form. They felt the format was not user

friendly. It was very long. And in order for them to read all the elements that the clinic staff felt they should read, they actually had to be coached through the form. So it involved a lot of time for the clinic staff to make sure the firefighters went through. And this just gives you an idea of how long it was.

The form was actually 10 pages long, which is really a long time. Firefighters actually just wanted to sign the form without reading it. And so clinic staff really needed to walk them through it to make sure that they learned about all the parts that they thought were relevant.

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DR. DAS: Even though FOX took place in an outpatient clinic where staff were knowledgeable about obtaining biological specimens, there were errors made during specimen collection. We learned that obtaining specimens in a clinical setting is quite different than clinical research.

The staff appreciated getting the illustrated protocols, which were different than what they were used to. Specifically, the serum processing required skills that the staff previously were not used to. They needed to use glass pipettes instead of plastic. They needed to use specific specimen containers. And these skills needed

to be learned and practiced.

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DR. DAS: Dr. Israel made some suggestions for improvement, including that the consent form be made reader friendly, and contain more white space and larger fonts. We need to weigh this against including all the required elements. Including white space and fonts, and bulleted text is great, but it means a longer document. There's no easy way to get around that informed consent form.

In addition, we realized that it's really important to provide very close training and oversight for clinic staff, no matter how experienced we think the staff are. And that extends to any other collaborating laboratory staff. Face-to-face training or video training is really optimal. We think that an early site visit is really necessary to observe that proper protocols are being followed. We think providing a hotline for clinical staff to call and ask about questions is really important. And it's important to include time and resources to make sure that proper lab practices are being followed prior to recruiting participants, to make sure that none of the specimens are actually compromised by inappropriate protocols being followed.

And we're using some of those lessons learned in

our upcoming projects that we're implementing in the field.

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DR. DAS: We think FOX was a success in spite of all these barriers that we identified. We recruited the participants. We obtained specimens. We didn't encounter the same obstacles that we did in MIEEP, in terms working in the labor and delivery ward. The firefighters were very willing to participate. We had a very high participation rate.

And at the last Panel meeting, the Scientific Guidance Panel encouraged us to capitalize on this success and to consider additional firefighter biomonitoring studies in other parts of the state. We also received public comment to that same effect.

And so following up on that advice, we've started some preliminary conversations with the San Francisco Fire Department, who's very interested in biomonitoring their members. And we're just thinking now about the future, and collaborating with other researchers in pursuing some biomonitoring studies, possibly with the San Francisco Fire Department.

Firefighters are very interested in environmental sampling combined with biomonitoring. And the types of sampling we might be considering include area sampling,

personal breathing zone sampling, and incident based biomonitoring, which is going to the site of an incident shortly, or biomonitoring shortly after an incident to see if the response to the incident has an effect on analytes. These are all possibilities and we haven't committed to anything yet.

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DR. DAS: Based on the advice from the Panel, we are also exploring the possibility of future collaborations with additional occupational cohorts, such as nail salon workers. We've had a preliminary conversation with Dr. Thu Quach and Dr. Peggy Reynolds, and are considering the possibility of collaborating with the Healthy Nail Salon Collaborative. And I'm hoping that possibly in the future there will be a presentation made to the Panel from those researchers, so you can weigh in on the possibility of collaborating with that cohort.

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DR. DAS: We are just getting into the field with our next pilot Biomonitoring Exposure Study or BEST, which is a collaboration with the Kaiser Permanente Division of Research Program on Genes, Environment, and Health.

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DR. DAS: You heard about this last time. Just to refresh your memory, we're planning to recruit 100

participants based on a stratified random sample of Kaiser Permanente Northern California members in the Central Valley. We'll be recruiting from seven counties listed here, and shown and highlighted on the map. And thanks to Dina Dobraca for making this map. It very nicely shows the geographic area for our sample.

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DR. DAS: Our phlebotomist was hired and trained just in the last few weeks. And this week we're training the Kaiser lab staff on our protocols based on the lessons we learned from FOX. The letters were mailed to potential participants. And their field visits will begin in the next few weeks.

The field visits will be a site visit to the participant's home with biological sample collection and making sure that they fill out a questionnaire that will have been mailed in advance. If the participant wishes to come to a Kaiser facility instead of their home, we will accommodate that as well.

This is the protocol for the first 10 participants. After that, we're looking to having electronic questionnaire administration and the process of sample collection will be reviewed.

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DR. DAS: At the last Panel meeting, I made the

presentation about this project, because Dr. Stephen Van Den Eeden from Kaiser could not be there, and there were several questions posed by the Panel Members. And I just want to take a few minutes to answer some of those questions, which I attempted to do at the last meeting, but we've gone back and verified the responses with Dr. Van Den Eeden.

The sample for this initial BEST collaboration will not include Spanish speaking participants. However, this is something that we are exploring for a future collaboration with Kaiser, and we'll definitely include Spanish speaking participants in the future.

This particular BEST collaboration will include people who are already part of the RPGEH database. In other words, if they've already contributed biological samples to the Kaiser research database, they could still be a part of this particular Biomonitoring Program.

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DR. DAS: There was a question posed as to why 55 was the cutoff. We're recruiting participants under 55 and over 55. The age of 55 was a random age just to separate younger and older age groups.

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DR. DAS: There was a question about home visits, and the cost involved. We had considered using the

laboratory order system for sample collection at a Kaiser facility. It was just not possible to implement that for this collaboration to get it into the field in the time frame that we wanted, but it's something we're looking at for the future.

Environmental assessments will not be part of this particular collaboration. It would involve additional funds. And so this is something we could consider in the future, based on the availability of additional resources.

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DR. DAS: And finally, there was a question about specimen quality control. We're planning to collect urine and blood and ship them overnight. There was a question posed as to whether shipping urine samples overnight would compromise the integrity of the samples and affect the analytes.

The Environmental Health Laboratory reviewed the literature and the sample integrity studies, and we've decided that storing and shipping overnight on ice packs would retain sample integrity for up to 24 hours. And if you have additional questions on that, Dr. She will answer that. And this pertains primarily to the urines.

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DR. DAS: A brief update on the public

involvement plan. Amy Dunn provided you an update at the last meeting. The Program is still in the process of finalizing the public involvement plan, which is being revised to reflect suggestions made by the Panel and the public.

These include more than 200 specific suggestions. The plan is also being updated to capture current work being done to prepare for reporting results to the FOX participants. Relevant findings from the March workshop on understanding and interpreting results will also be incorporated into the revised plan.

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DR. DAS: While day to day activities really take up the bulk of our time, we're also very conscious that we need to do some long-term planning for sustainability and success.

We had a day long meeting in April, where we began a strategic planning process. This included starting the development of a shared vision and a long-term strategic plan. We invited input from all Program staff and considered the input that the Panel members provided at the March meeting.

As a result of the meeting, we now have monthly meetings between the program leads, which are Dr. She, Dr. Petreas, Dr. Jed Waldman, who's the Branch Chief for the

Environmental Health Labs and myself and Sara Hoover from OEHHA.

At those meetings, we further develop options for program sustainability, and criteria for future projects, and also talk about improving day to day tasks such as tracking lab tests and other work. We bring those discussions to the larger meetings that we have with all Program staff twice a month.

This week we also had the first of what we hope will be quarterly calls with the two other CDC funded biomonitoring states, New York and Washington. This is a call that's primarily between the lab staff to compare methodology and expertise, but I think there are lessons we could all learn from those calls.

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DR. DAS: And finally, we are engaging in a few additional activities. In 2010, we submitted our first required report to the Legislature and we are currently working on the second report, which is due in January 2012.

Last time the Scientific Guidance Panel provided some recommendations which we found very useful. And we're hoping that at this meeting the Panel will also provide some recommendations that will benefit the Program.

We're completing our CDC annual report as we do every year. And I just wanted to provide you an update on the National Biomonitoring System Guidelines, which I had mentioned at a previous meeting. The American -- the Association of Public Health Labs, APHL, has begun an effort to make biomonitoring more recognizable to the nation as a whole and to start a national biomonitoring system, which is biomonitoring capacity, capability in every state.

The collaborating organizations include APHL, Association of State and Territorial Healthy Officials, ASTHO, and the Council of State and Territorial Epidemiologists, CSTE. Together these three organizations provide laboratory, policy, and epidemiology expertise.

And I've participated on the CSTE Committee. And together with the Minnesota staff, Jean Johnson in particular, in developing the CSTE guidance for these organizations. We're nearing the completion of these three guidance documents and we hope that they'll be released in the near future and provide guidance to states that are considering developing biomonitoring programs.

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DR. DAS: Finally, we could not have this complicated Biomonitoring Program without the assistance of many, many people, the village of biomonitoring. And

I'd like to extend a big thank you to all the staff whose work is reflected in this presentation.

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DR. DAS: And also to the various collaborators including the SGP members and our collaborators outside the Program itself.

Thank you very much. And we have time for questions.

CHAIRPERSON LUDERER: Thank you very much, Dr. Das. And once again, I'm impressed with all the progress that the Program has made with the limited resources that are available.

Do any of the Panel members have any questions or comments for Dr. Das?

Dr. Bradman.

PANEL MEMBER BRADMAN: Well, I think just -- I'm sure this is probably echoed through many in the room, just the value in biomonitoring, in this case identifying the elevated mercury exposure and the follow up. I think that's a good example of the potential public health benefits of this program.

In this case, we had a compound that had CDC guidelines and procedures for follow up, but I think everyone probably nodded their head and said that was a worthwhile -- well, not worthwhile, but that was a find

that I think really underscored the value of the Program.

DR. DAS: Thank you, Dr. Bradman. I should also mention that beyond the organizations that I mentioned at the local State and federal levels, we also work with other partners in the Department of Public Health including our Food and Drug Laboratory Branch who did the analyses for screenings and other products that we tested. So it was truly not only a public health success, but a great collaboration as well.

CHAIRPERSON LUDERER: Dr. McKone.

PANEL MEMBER McKONE: Just following up on the mercury. It actually -- I think you brought this up. I think we want to focus a little bit on the lesson it gives for the stratification of samples as we build the Program to represent different populations. I mean, I know this is a challenge for CDC, but here's a case where it's actually a relevant -- it's not a really large -- it would have been hard to find through a random screen. I think, you know, it's the factors that made it show up. But I think it does point out that there are going to be chemical substances or other substances that may be very high in a relatively small subgroup, that if we don't know how to stratify our samples, and we just do like a random sample, the way you would for a political poll or something, you're going to miss the hot spot or a group at

a high level.

I just think we have to be aware of that kind of challenge in building a sample strategy.

DR. DAS: I think that's an excellent point. The fact that we were able to identify this case had to do with the population that we focused on for the maternal infant project, and also the substance. The use of mercury in face creams is actually fairly widespread among a number of different ethnic groups. And there have been reports from all over the U.S. that highlight that issue.

But I think if we had done a small random sample, we may not have been able to pick it up. So your point is well taken on that.

CHAIRPERSON LUDERER: Dr. Quint.

PANEL MEMBER QUINT: Julia Quint. I also want to just echo. It's so impressive, particularly not only the work that you've done with limited resources, but the lessons that are being learned from the smaller studies that will service us well, when and if we have the resources to do a larger study.

And in that vein, in several of the studies you identified them as barriers. And, you know, they're also a positive in the terms -- in the sense that we won't have to learn those lessons again for a larger study, but they've required -- they seem to require increased

resources. You mentioned the hotline. You mentioned video training and in-person training for clinical staff, which was surprising to me. I would think that clinical staff would know how to handle all specimens, but certainly not true.

So I'm just wondering about the impact of -- you know, in terms of at some point, you know, sort of identifying whether or not this is going to mean that we might want to just highlight the need for some additional resources should those become available anywhere, you know, based on what we're learning from these smaller studies. And one other thing, you mentioned chemical specific information, which I think is really important to be developed for MIEEP project.

And I'm wondering how transferable those specific -- that information will be for other studies, I mean, in terms of the same chemicals or the same analytes being measured. You know, are we going to have to have specific chemical information per project, or, you know, I'm sure we can use some of the information, but it sounds like for some of these projects there's going to be a need to have information, not only for the participants, but also for health care providers and things like that. So I don't know if you know, at this point, how transferable they will be between projects.

DR. DAS: So in response to your first comment about resources. Yes, the interaction with clinical staff and partnering laboratory staff has been extremely labor and resource intensive. And so far, we've managed that by people just working very hard to interact.

As our project expands and we take on more projects, we hope that we'll make the processes more efficient. And knowing things in advance will maybe decrease the amount of work involved, but it does highlight the fact that we do need staff dedicated to interacting with our partners, and I think highlights the point that you made about the need for additional resources.

With regards to your question about whether materials that are chemical specific and made for one project are transferable to another. Certainly that's the way we've been approaching the issue with our partners across the Departments. We're working very close with OEHHA to develop chemical-specific materials. And while we may start with one project, because that's the first one that we're developing materials for, we're certainly looking at the issue as something that's transferable to other projects.

As I mentioned, we'll be doing usability testing for FOX. And that usability testing really tests the kind

of language and the education level that might be relevant for a particular population. But the scientific information that goes into different materials certainly should be very similar. And we're hoping that we won't have to do a lot of changes from one project to the next. But I think the usability testing that we're about to conduct will help us to figure out how transferable materials are from one project to the next, and also we'll find out something from BEST as well. So the intent is that we will make the chemical-specific materials transferable and not have to redo them for every project.

And, Sara, did you want to add something about that.

MS. HOOVER: Yes. Sara Hoover, OEHHA.

Just one other little note on that. We are checking if there's a certain tailoring that might be needed, like, for example, the firefighters, we looked for special firefighter exposures in that case.

In general, though, we are able to keep it very similar. And then ultimately the goal, we're actually embarking on a kind of major reworking of the website with some funding from CDC. And ultimately, the goal will also be to get that chemical specific information on the website.

CHAIRPERSON LUDERER: Dr. Solomon.

PANEL MEMBER SOLOMON: Yes. I just wanted to echo the comments of other Committee Members. Very impressive progress since the last meeting. And I may have missed this, but when you talked about the staffing changes and the vacancies. Are those vacancies -- are you -- have you been given the green light to proceed with those hires or are those in someway tied up with hiring freeze issues or budget issues? It would just be helpful to know.

DR. DAS: Within the Department of Public Health -- I can't speak for the Departments, because we have slightly different approaches. But the State as a whole does have a hiring freeze. We have a process whereby if we want to hire someone, we have to request an exemption to the hiring freeze. And it -- unless, we get the freeze exemption, it does make it difficult to hire into the position.

So each position is handled individually. And so our ability to hire into a particular position would depend on whether the freeze exemption is granted for that position, as well as who the candidates are. Certain positions can -- are easier to hire into than others.

PANEL MEMBER SOLOMON: And have freeze exemptions been requested or granted for the two research scientists and the research scientist supervisor positions?

DR. DAS: I'm in the process of requesting a freeze exemption for the research scientist that's in the Department of Public Health. Regarding the research scientist supervisor --

DR. SHE: For the research scientist -- this is Jianwen She, Chemistry Section Chief. And for the research scientist supervisor position, we also have a process to request an exemption.

MS. HOOVER: And for OEHHA's research scientist position, we've been given internal approval to write such an exemption request, and we'll be working on that.

CHAIRPERSON LUDERER: Okay. Are there any other questions from Panel members at this time?

If not, we can move on to public comments. Did we receive any requests from the public to speak?

MS. DUNN: One in the room and one from Email.

CHAIRPERSON LUDERER: It looks like we have two. One from the webcast and one here in the room.

Do we have a card for the -- oh, okay. Great.

CHAIRPERSON LUDERER: We'll start out with the member of the public who is here in the room. This is Mr. Davis Baltz from Commonweal.

MR. BALTZ: Good morning, Davis Baltz of Commonweal. Nice to see all of you again. And I would also like to add my congratulations to Dr. Das and the

Program staff for the significant progress that's been made. And has been noted repeatedly, over recent years, accomplishing quite a lot with resources that are less than was initially anticipated that the Program would have.

So I particularly took note in your presentation about others have mentioned the flagging of the high mercury in the MIEEP program. And a couple things that stuck out for me was, one, that you acted to develop a health alert in both English and Spanish. And that I'm sure was read and used by many.

And the other observation was that as a face cream that came in hand luggage from Mexico, this product escaped probably any kind of regulatory scrutiny that we might have in the U.S. But the point goes that I feel still holds that we have a lot of consumer products that have chemicals of concern in them, and we, even in this country, if it's not imported in hand luggage, we don't have an idea, in many cases, what the ingredients are, and we really actually need that.

And this kind of is a sort of side effect of the Biomonitoring Program, in that it can identify potentially problematic ingredients in chemical products, and contribute to one of the stated purposes of the Program, which is to both assess public health efforts to reduce

problematic exposures. And if we don't know what they are, we obviously can't take steps to implementing kind of regulatory actions. So the fact that this -- the MIEEP program discovered this just points out the value of biomonitoring.

And similarly with the FOX project, I'm impressed that you are tailoring responses for the population at hand. It shows sort of the extra care and diligence that the program is devoting to developing these materials. And the clinical collection process that the staff needed to be actually trained to using glass pipettes over plastic.

And it struck me that I'm sure plastic is sort of the standard these days. But in this particular case, we needed to use glass, because presumably the plastic pipette would contaminate the sample. And again, it points out to the wide spread exposure that we have in the health care setting and elsewhere to chemicals that we may not know enough about.

So we look forward to the further progress of the program. And in particular, when you're ready to release the results publicly for both MIEEP and FOX, I'm sure the nonprofit and NGO community will be eager to publicize those results, and perhaps add our own messaging to them specifically with the value of biomonitoring in

California.

So thanks again for all the progress.

CHAIRPERSON LUDERER: Thank you very much for that comment. I'm going to read the other comment that came in over the webcast. This is from Tim Shestek at the American Chemistry Council. And he actually has a question which is, "Is the results reporting form template developed by Dr. Morello-Frosch available for public review?"

DR. DAS: Rupali Das, California Department of Public Health.

Dr. Morello-Frosch made a presentation at the previous Scientific Guidance Panel, and the materials that were provided at that meeting are available for public review. The template itself, I actually don't remember what materials were submitted. So whatever is available for public review was made available at the previous Panel meeting.

MS. HOOVER: Yeah, in her presentation -- sorry, Sara Hoover OEHHA. In her presentation, she showed examples of what the template had looked like and how it improved. So it's not the complete set of materials, but it's a good representation of it. So I can actually provide the link after the meeting.

CHAIRPERSON LUDERER: Great. Thank you.

We now have some time for more Panel discussion and recommendations about this update, Program update.

Do any of the Panel members have comments?

Dr. Solomon.

PANEL MEMBER SOLOMON: Gina Solomon. I was just -- I find this mercury case or mercury situation intriguing. And there are a number of clinics that serve primarily, you know, Latino populations that may be affected by these -- the sales of these types of skin products.

And there was a study done by the Chicago Tribune that purchased skin screams from stores and found a high rate of mercury contamination in commercially available skin creams, skin lightening creams, blemish reducing creams acne creams, et cetera, that were sort of usually imported from Mexico, but not in hand luggage. So I think it's a broader issue than just, you know, a few folks.

So one possible follow-up project could involve partnering with some community clinics and doing, you know, a slightly broader biomonitoring study. And I'm sure there aren't resources available for that, but I just wondered whether there was any thought about doing something like that.

DR. DAS: Rupa Das, Department of Public Health. That's a very good suggestion. If we were to focus on

mercury, that is certainly something that we could consider all other benefits to biomonitoring as a whole.

As you mentioned, it is a matter of resources. So if that was something that we decided was going to be a programmatic focus, I think that would be a very good population to partner with.

CHAIRPERSON LUDERER: Dr. Quint.

PANEL MEMBER QUINT: Yeah. Julia Quint. Sorry, I have a frog in my throat.

One follow up I think which would be very appropriate, would be to ensure that the green ribbon science panel or DTSC and that whole effort is aware of, you know, this finding. And given what Dr. Solomon said about commercial products, also may be having inappropriate mercury content.

That would be a possible way of helping to prioritize consumer products within the green ribbon science -- well, that whole effort in terms of the regulation. So I think that's another good nexus between these programs that should be highlighted, in terms of, you know, the annual report or whatever to just show that findings from this Program can relate very much to the primary prevention effort that's going on that will go on in that program.

DR. DAS: Thank you for that suggestion. And I

think that's an excellent follow-up action that we can certainly take to provide this information to the green ribbon panel.

CHAIRPERSON LUDERER: Any other questions from other Panel members?

I did have a question, you mentioned the funding situation that you're waiting to hear from the CDC about the upcoming years of funding. And I was wondering whether you had any information about the TSCA funding for 2011-12?

DR. DAS: I don't have any information to indicate that it would be any different, but we can certainly follow up on that.

CHAIRPERSON LUDERER: Good. Okay. Any other recommendations, discussion from Panel members?

All right, then we can, if not, move on to the next set of presentations and Dr. Das will introduce Dr. She and Dr. Petreas.

DR. DAS: Our next speaker is Dr. Jianwen She, who is the Chief of the Biochemistry Section in the Environmental Health Labs of the California Department of Public Health. And he will be followed by Dr. Myrto Petreas who is the Chief of the Environmental Chemistry Lab in Department of Toxic Substances Control.

Dr. She.

(Thereupon an overhead presentation was Presented as follows.)

DR. SHE: Thanks, Dr. Das for your introduction. And good morning, Scientific Guidance Panel members and conference audience.

I will update you now with the Environmental Health Laboratory's progress from the last four months.

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DR. SHE: First, I will update with new staff change. As Dr. Das mentioned, we have four laboratory interns. And they are in the audience. And Anthony Zhou and Austin Long is helping with PAH methods sample preparation in the laboratory. John Li is helping with phthalate sample preparation. And Sherry Wang is working on dry blood spots and the dried ultra low volume of blood. We talk about the 50 microliters samples.

And while we are welcomed with these new energetic interns, who will be our next generation of environmental scientists, we also lost two experienced staff as Dr. Das mentioned. Frank Barley retired at the end of June. And Mr. DaSheng Lu returned to the CDC -- Shanghai CDC. Their departures are a big loss to the laboratory.

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DR. SHE: Moving into the laboratory equipment,

we are currently planning to purchase another LC-MS/MS for perchlorate analysis. And hopefully this machine can be also used for unknown compound identification and confirm any target compounds. We are evaluating three options at this moment.

Also, in the last four months, we installed a Zypher Solid Phase Extraction Workstation. We hope this workstation will help us to automate sample preparation, improve the precision and decrease the time and the labor needed for sample clean up.

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DR. SHE: At the same time, we have continued to develop methods, validated methods. And along with this effort, we use the validated method for the production, which I need for the MIEEP, FOX study sample analysis.

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DR. SHE: These two new methods -- these two methods are still under development. One is metal panel in urine by ICP-MS. The second one is arsenic and mercury speciation in urine by LC-MS. And I do not have so much progress for these two methods at this moment. Hopefully at the next meeting we will have more update on these two methods.

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DR. SHE: Currently, we have three methods under

validation. One method is dry blood spots. And the other method -- actually, similar method works low volume of blood, as it related to dry blood spots. So that low volume will be called dry blood spots volume, roughly 50 microliters to 100 microliters.

Also the hydroxy-PAH by GC High Resolution MS and the hydroxy-PAH, by LC-MS/MS.

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DR. SHE: For the DBS method, as I mentioned at the March meeting, SGP meeting, we face a few challenges. We have very low sample available -- very low volume of sample available. Also, due to the filter paper, the analytes is very hard to extract and recover. So to solve the first challenges for the low volume samples, we maximize instrument sensitivity.

And then to address the second challenges, basically we eliminated clean-up procedure, because we have very low volume of sample analytes concentration -- amount was so low. If we have multiple steps for clean-up, analytes will be lost with that clean-up.

So we basically developed a method without any sample clean-up. We hope this DBS method can be used for samples collected by California Newborn Screen Program, and the DBSV method can be used for the California maternal serum alpha-fetoprotein screening program.

And also both methods can be generally used for less invasive collection methods, for example, finger tip blood collection.

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DR. SHE: So basically we call it the one-drop blood method. So they actually inject blood into the system, we need to evaluate the system performance because blood is a very complex matrix. The matrix effects may interfere in our analysis.

So this slide shows after hundreds of runs, we still have a very symmetric peaks, as is shown on the top. And then the baseline at the bottom two graphs shows we have very clean baselines. So the system can handle the samples without clean-up.

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DR. SHE: The top slide shows line 14 PCB and the 5 PBDE. We start with PCB and the PBDE first. We hope we can expand the method to other analytes. New York used the DBS for PFOS chemicals to do the time trend and the CDC worked on the DBS on the perchlorate.

Now, let's check our method of performance for this low volume and dry blood spots. Column 2 and column 4 show us -- show you the recovery we get from this method with blood sample at the 0.16 micrograms per liter. And we have a very reasonable recovery. DBS the recovery is

good. DBSV recovery even better.

And also column 3 and the column 5 show the precision of the method. The same was true DBS have very good precision and the DBSV even better.

The last two columns show we have satisfied accuracy. And you can see the last column is certified values. Our DBSV values matched with certified values.

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DR. SHE: The most challenging part of our Fogarty staff Mr. DaSheng Lu develop this method left. Now, we have Sherry continue this process.

A lot of the method we validate the hydroxy-PAH by High Resolution GC-MS and also hydroxy-PAH by LC-MS/MS method.

The reason we did the two methods, because we start with hydroxy -- GC-MS method, we notice some problems. And sometimes, especially High Resolution GC-MS it required a very skilled operator. We not necessarily have them always with us, so that's why we started a second method LC-MS/MS.

But this slide shows you with our High Resolution MS method, the last column show you after 20 runs, our precision is very well. And the only problem was with the two naphthalenes, 2-hydroxynaphthalene our precision is slightly high. But for all of the others our RSD is below

15 percent, which is very good.

And we are still validating with the external reference materials for the accuracy at this moment. LC-MS/MS method is almost similar. We hope at the next meeting we can put these methods for production.

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DR. SHE: I'm very excited about our progress in the last two years, especially after CDC funds. We are able to bring six panels of chemicals into the production. For example, metals in blood, and phthalate metabolites, OP common metabolites, OP specific metabolites, environmental phenols and the creatinine.

OP common metabolites and environmental phenols are our newest method for -- in production. And just a reminder for everyone, we created this lab from scratch. So in two years, we bring this capacity up. And I really wanted to thank all of the dedicated staff and our funding agencies who make that happen.

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DR. SHE: Along with our method of development and other activities, we work on the sample analysis to support MIEEP and FOX studies. The last column shows how many samples we analyze at this moment. So we are 100 percent through all of the metals requested from both studies. The exciting part, the laboratory find a high

level of the mercury, as Dr. Das reported already.

We are halfway through OP specific metabolites and the creatinine analysis, and a quarter of the way through OP common metabolites and the environmental phenol analysis. So we are confident that we are on track to finish all of the analytes for both studies on time.

We are about to start analysis of the phthalates and the PAH in the next one or two months.

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DR. SHE: Thank you

CHAIRPERSON LUDERER: Thank you very much, Dr. She. It's very exciting to see these new panels of analytes coming on line. Congratulations for successfully bringing those into production.

Do any of the Panel members have questions or comments?

Dr. Bradman.

PANEL MEMBER BRADMAN: I have a comment and a question once again. Just to echo the previous comment, really great work and lots of progress, and very impressive.

I had a question about the DBS and those methodologies. One I want to say that I think that is really exciting information. I mean, this is tremendously important and is potentially a huge resource to take

advantage of this extensive, you know, blood collection that's occurring and can really, I think, influence both, you know, biomonitoring and epidemiologic studies and really provide a lot of good public health information for the State and nationally.

So I just want to underscore, I think that's a really great and important effort.

I also had a question. I'm wondering if maybe another step in validation might be to take some individuals and volunteers and collect some blood and spot some of the -- and basically collect some blood spots from an adult, where you have, you know, blood collected by venipuncture and then blood collected on a dry -- in a dried blood spot method, and then compare the results, particularly for things like the BDE-47, 99, the ones that are often -- you know, we know they're going to be present, and that way it would be another level of validation beyond the spike and recovery studies.

DR. SHE: Thank you, Dr. Bradman. So the suggestion is we validate our method with the new method and the traditional method, is that it?

PANEL MEMBER BRADMAN: Exactly.

DR. SHE: I think that's a very good suggestion. Dr. Myrto Petreas and I discussed a similar idea, and she collected about 10 samples. And we prefer to finish them.

We've kind of new sample analytes. Yeah. So we will follow-up with that suggestion to further validation.

PANEL MEMBER BRADMAN: Yeah, I think that would be a great next step. And again, just to underscore the real value of this work for California and nationally. This is a tremendous resource that's very important to develop.

DR. SHE: Thank you.

CHAIRPERSON LUDERER: Dr. Quint.

PANEL MEMBER QUINT: I just want echo that. Julia Quint. Just tremendous gains. I have a question about the blood spots as well. You mentioned that -- will we be able to use existing samples from newborns with this methodology? Is there an existing source of samples to which this methodology can be applied in addition to, you know, just future analyte detection and new samples? I was unclear about that. I heard something about newborns, and I know that, you know, we routinely conduct certain tests on newborns, and I'm wondering if we're able to tap into those samples, in terms of our biomonitoring effort.

DR. SHE: Ideally, if we can use archived samples --

PANEL MEMBER QUINT: Yes.

DR. SHE: -- collected by the newborn screening program. And for that effort there are other two

challenges. One is the possible contamination of the first people. When the newborn program started, they screen the paper for the new assay and all of the other metabolites. We didn't screen the paper with -- for the, example, PCB and the PBDEs.

So we did some work to try to test the paper from different years in the laboratory. We think that's possible we can use the newer, for example, after 1992 the paper collected is possible we can use this archived sample after 1992 with some background subtraction and -- but for maternal serums I'm sure we can do the archived samples. Yeah, at least from material serum for this moment.

And the method to apply from now on for the newborns screening, we may need to work with newborn screening program to see if we can screen some of the paper for the future use.

PANEL MEMBER QUINT: So does that require a consent mechanism, or do we automatically -- can incorporate that into the program?

DR. DAS: Rupa Das. We've had some preliminary conversations with the genetic disease screening program, which houses both maternal serum and infant blood spots, in order to -- our preliminary conversations suggested that we would not need a consent. However, we're really

waiting to see if we have the methodologies before we pursue an actual agreement to obtain the samples. And at that point, we'd have to probably go through some sort of process in order to determine which samples we would take and determine how we would access the samples.

PANEL MEMBER QUINT: That's great. I just had a separate question about the hydroxy-PAHs. You mentioned two different instruments, I don't know if they're different methodologies, but two different methods, but two different instruments. And I'm wondering what the -- why you need to measure them in two different ways.

DR. SHE: Yes. We started a follow-up of CDC procedure, which is GC High Resolution MS method. As I mentioned, this machine is in certain ways not a high production machine. Each run take like 30 or 40 minutes, and the machine is very volatile. And to make it reliable, it's not so easy. And we are aware CDC is to move away from it too. They're moving to -- from the High Resolution GC-MS method to the GC-MS/MS method this moment.

And since we follow them, so we don't want to stop this procedure, because that's considered the golden standard method of sensitivity. No other machine can compare.

We run 20 runs. Within each run, we fail of new

samples. So we cannot afford to fail the patient sample. We can fail the testing. So right now, I think we validate the method for precision with GC-MS, but we kind of feel is this good enough to real samples. And at the same time, we have a resource to develop an LC-MS/MS method.

So that method will come up very closely and at the state -- stage to be validated. I hope in the next three months we can see which one turns out to be better.

PANEL MEMBER QUINT: That's great. Thanks.

CHAIRPERSON LUDERER: Do any other Panel members have questions?

I actually did have a question about the dry blood spot testing. I also think that's extremely exciting. I think that's such a huge leap forward and I'm really looking forward to hearing more about that in other Scientific Guidance Panel meetings in the future.

You know, one question that I had, and this is just -- it's about your method performance data. And one of the things that I noticed is that the recoveries a lot of them seem to be greater than 100 percent. And maybe this is just my lack of understanding, but you had mentioned the filter paper, that there might be some contamination. I was wondering if that might be reflecting that or is there some other reason.

DR. SHE: Okay. This recovery ideally you want it to fall between 70 and 120 percent. So your concerns for some of them will have 124 percent. For example, PCB 118 with a dry blood spots would have 124. And then also BDE-153, we can't handle 140 percent of recovery. So these two we still need to work on. It's 140 percent may be out of the reach. 124 is on the boundary.

But this is a sample we only take one spot is about 50 microliters. Most of the state right now they use a pooled spot, most other researcher. So if we able to pool two spots together with a volume of about 100 microliters, we maybe able to improve that 153 BDE recovery. So that's a good question. So we do still have work to do to make sure every single congener can be measured exactly.

CHAIRPERSON LUDERER: Thank you.

DR. SHE: Thank you.

CHAIRPERSON LUDERER: Dr. Alexeeff.

OEHHA ACTING DIRECTOR ALEXEEFF: Yeah. I have one question. On the hydroxy-PAHs, I was just wondering what medium the samples were in?

DR. SHE: Oh, that's urine. Urine samples.

OEHHA ACTING DIRECTOR ALEXEEFF: Okay.

CHAIRPERSON LUDERER: Okay. Shall we move on to the next presentation then, at this time?

Thank you very much, Dr. She.

(Thereupon an overhead presentation was Presented as follows.)

CHAIRPERSON LUDERER: Dr. Das, if you'd like introduce to Dr. Petreas.

DR. DAS: The next speaker will be Dr. Myrto Petreas, Chief of the Environmental Chemistry Lab at the Department of Toxic Substances Control.

DR. PETREAS: Good morning. I'm very happy to be back with you again, and update you on where we stand in the DTSC lab, if I can find my slides.

Okay. This will be an update for our labs which focuses on serum. We have to differentiate, no urine here just serum.

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DR. PETREAS: So today I will give you an update on where we stand on our capabilities for analyzing chemicals on the priority list that we have discussed, where we stand with the field studies, FOX and MIEEP, other activities we performed that benefit the Program - these are our success stories - and also the challenges we face.

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DR. PETREAS: So starting on where we are with methods. We now have validated methods and we have the

capability and capacity to perform analysis for the persistent organic chemicals classes, such as the PCBs, polychlorinated biphenyls, organochlorine pesticides, polybrominated diphenyl ethers, the PBDEs.

I'll stop here. Those three classes we're able to measure in the same sample of serum. And this is very significant and very important restriction for us. We have very limited and very precious serum samples. So we're trying to do all these analyses in the same specimen, one to two milliliters depending on where we want to finalize the method.

So we're successful so far to literally extract everything out of that one milliliter and get the three first classes. Having that method, we tried to tweak it and tried to see how much can we add on. For example, from the bottom line, some of the selected brominated organic compounds used as flame retardants from the priority list, we're able to add some of those chemicals onto our persistent organic chemicals methods.

Separately, with a separate sample, aliquot, and a separate analysis are the perfluorinated compounds, the PFCs. So, so far, in this slide we show what we can perform as we speak now and we're still expanding.

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DR. PETREAS: These are the specific selected

brominated organic compounds used as flame retardants that we're able to add into our method for the persistent organics. So I'm not going to read all of them, but these are the ones that we can include and we have methods right now.

Separately, the last bullet is tetrabromobisphenol, TBBPA, another very important flame retardant. We have a method for that. This is done separately. This is done by LC-MS. Everything else was -- our initial robust method was GC -- High Resolution GC-MS. So we have that method and now we're starting to perform with LC.

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DR. PETREAS: A concern -- actually we'll go back and -- even though we have methods for these flame retardants, it took us a lot of time to tweak our original method to include them. And our quality control is very good. Whenever we spike in our test method, we find. When we analyze real human blood samples, we never see any of this.

So we're a little puzzled and frustrated, because either our method is not as good as we think or these chemicals are not really measurable. It's hard to say. Nobody has performed or reported these analysis in human blood. So we're a little frustrated on whether it's

really worth making our method either so much complex to try to measure these chemicals, if maybe these are not measurable. Maybe these chemicals -- we're looking at the parent compounds. These are the compounds we're measuring.

Maybe they're metabolized. Maybe we should be looking at something else. There's not much information on pharmacokinetic. There's not much information on analytical methods. And, frankly, we haven't seen anyone reporting on human data for these compounds. They're in sediment. They're in dust. They're in -- they are there, but whether they are absorbed or present in the blood, we don't know.

So that's something we want to, at some point, decide, whether we should forge ahead and include these in our methods, before we go into the field studies or just drop them and be more efficient and effective and stick with our previous persistent organic chemicals.

In addition, there are other -- this long list of selected brominated -- this slide should say brominated and chlorinated organic compounds. These are all the chemicals in alphabetic order that are on the list and we have no capability yet.

Now, these are very disparate chemicals. They're not even common classes. They're very different. They're

phosphates. They're chlorinated. They're paraffins. And each one of them may require a very different method. Some require high resolution mass spec. Others would be more amenable to LC-MS.

We have some plans to start with, for example, the polybrominated biphenyl 153, the Fire Master -- the original Fire Master compound. That's our next on our list to try to include and some others. But it's a long list and we're not sure how successful we'll be and how much time we need to devote on those. And to complicate things, there aren't even commercially available standards to make sure that what we see is really what we think it is. So it's a big long list ahead for us on that

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DR. PETREAS: Sorry. Okay, yeah, I'm highlighting the ones that we think we can make.

Okay. Now, some success story here. We're very thankful for being part of the CDC cooperative grant. And with their funding we've purchased an LC-MS/MS last spring. Staff were trained. It's in production. I'm very happy to report that we now are using this new LC-MS for a panel of phenols in serum.

So we have a method, as I said, on the tetrabromobisphenol A, TBBPA. We have BPA, bisphenol A and some of the tribromo or dibromophenols in blood. So

this is in production.

And our next goal is to add triclosan and the PCB and PBDE hydroxy-metabolites. And the other flame retardant, hexabromocyclododecane. And I should say that the hydroxy-metabolites, we have methods currently, but they require GC-MS. And for that, they require derivatization, which is a very nasty chemical process, that we want to avoid for safety sake and efficiency. And we tried to include those classes of very important metabolites into our LC-MS. So that's the way we want to go with the LC-MS.

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DR. PETREAS: So to summarize, we need to have a very sensitive method. We have very small volume of human serum. We need to have very low detection limits. And now we can -- with one injection, we can do the TBBPA, the BPA and the bromophenols. And the question is can we -- oh, sorry -- there goes my animation.

So the question was can we add those other chemicals, the brominated flame retardants and the hydroxy-metabolites in one sensitive method.

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DR. PETREAS: Moving on to where we stand on the FOX and MIEEP studies, we have -- when we receive a sample to do batches from the Richmond lab. So DPH receives all

the samples and we receive them in several batches, we want to minimize the number of thaw and freeze cycles. So we try to time when we aliquot the samples to separate how much we need for the persistent organics, for the perfluorinated and for the lipids. The lipids will be sent to a clinical laboratory in Boston for that.

So for the FOX study, we have aliquoted all of the samples and we have performed all the PFC analysis for all the samples. And we're just starting to do the persistent organics. So 100 percent done for the PFCs and about 10 percent for the other classes for the FOX.

The MIEEP, the 140 samples, we have aliquoted half of them. Oh, no, sorry, about a third of them. And we have done a few of the PFCs. We're very concerned because, as you know, cord blood has very different -- it's a very different matrix. First of all, it has very little lipids. It's about a 5th of the lipids -- 20 percent of the lipids that is present in serum. So we weren't sure what we could see, but we're happy to report that in these first batches that we run for maternal and cord blood, we were able to see all the PFCs in our methods. So we should soon have results for those.

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DR. PETREAS: Now, I want to give you an update on other activities that are funded from our Department or

through other extramural grants, but they are of benefit to the Biomonitoring Program. And what we learn from those, we can apply to our biomonitoring studies.

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DR. PETREAS: We have a study funded by the Breast Cancer Research Program. It's a teacher's study. This is a long ongoing longitudinal study of teacher -- breast cancer in teachers. And the study was recently funded. We have to measure persistent organics and perfluorinated chemicals in blood of contemporary samples. So women will be sampled now.

The questions we were faced with is can we have more flexibility in the field. In this case, field staff will be visiting the teachers in their homes or work places, and among other things collect blood. And because of the non-proximity to a facility, it may take time before the blood can reach a laboratory before it can be processed.

A secondary question is, that study has a lot of archived blood samples, are they still usable?

So the question is how long can samples be stored frozen? So for that, I should give you a little background. The traditional method is what's called Red Top. This is a Red Top tube, where you draw the blood, but that requires -- this is not anticoagulated. So you

let it clot. And then it needs to be centrifuged and processed within 24 hours. This is the standard method.

Processing means opening the tube transferring it to another tube, centrifuge again. So it requires a really clean environment and a safe environment for staff.

The other option is a Serum Separator Tube. And this requires only centrifuging in the field before it can be frozen, then shipped.

So the question is, is the SST equivalent to the RT?

The other thing is how long can we wait? The standard method again is we have to do it quickly, but can we really stretch our limit to 48 hours, because sometimes staff will not be able to return the samples within the 24 or 36 hours.

And the other question is, two years freezing is that affecting the samples versus the shorter period that we usually have?

So for that we conducted pilot study.

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DR. PETREAS: And we drew blood from 11 volunteers, who all of them gave six tubes, still within IRB approved protocols. So six tubes, three of each kind. And we had this scheme where we processed them at different times, either two hours or 48 hours. And we

stored them for one month, and analyzed them for the persistent organics, pesticides, PCBs, PBDEs, PFCs, some of the BFRs and the lipids.

I'm happy to say that with some elaborate statistical analysis that our collaborators performed, you can see there's no difference between the 48-hour Serum Separator Tube and the standard two-hour processing of the Red Top.

So this is a major breakthrough, not only for the teacher study, because we are using now the Serum Separator Tubes in the field, but this is something we can use possibly with the BEST study with Kaiser, which may require again field staff to go and visit participants in their homes. So that's a possibility we can explore. So I think we're very happy that we have this opportunity to study that.

Now, we still have two tubes stored in the freezer that we'll analyze in two years to try to answer the other question.

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DR. PETREAS: Another collaboration that we have with the University of Cincinnati this time will help us a lot with the MIEEP study. So we were asked to analyze 10 pairs of maternal serum and cord blood exactly like the MIEEP study, for PBDEs and the hydroxy-BDEs for

metabolites.

So the very important findings that we did find all the congeners. They were measurable, not only both in serum but also in cord blood. So our concerns about lipid content, because these are lipid soluble compounds, is not an important concern. So we hope that we will be able to see all the chemicals in the MIEEP study.

The interesting thing we found is that hydroxy PBDEs in the cord blood were higher than the maternal serum, when we did a paired analysis, which means that fetuses may have even higher exposure.

And to show this a little graphically here -- by the way, this we will be presented, I think, in the fall in the ISCS conference.

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DR. PETREAS: So if you see the left-hand side bar graph, this shows mothers to the left and cord blood to the right. PBDEs, these are the sum of PBDEs, are in blue. And in maroon are the hydroxy-PBDEs. Note that the scale and the units here nanograms per milliliter of serum. So they are not corrected for lipids. And that's done to see how different the mother and the babies are, in terms of the ratio of these two.

Usually, we expect what you see in the mothers, like the hydroxy-metabolites are lower than the parent

compound. This is not true in the babies. Now, again, PBDEs are not reported, not lipid adjusted. So on the right-hand side in the dark blue bar graphs, we show the lipid-adjusted PBDEs, which are the usual way of presenting them. And there the data are not significantly different. But again, as when we did the analysis of pairwise, we saw the babies had much more than the mothers.

So again, very limited data, only 10 samples so far. We're going to do more with them. And that will help us put in perspective what we find with the MIEEP study.

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DR. PETREAS: Another study we are collaborating with UC Berkeley is the household dust. This is with the childhood Leukemia study with Pat Buffler and her staff.

So in our lab, we are analyzing dust from vacuum cleaners. A little background, if you remember, by 2006, penta and octa-BDEs were restricted or banned. And penta-BDEs are used in furniture and furnishings. Where as the octa-BDEs are in electronics. The other major class are the deca-BDEs and these are continuing unrestricted.

So in this study, 204 houses of children with and without leukemia had their vacuum cleaner dust sampled

twice. The first phase was between 2001 and 2007, and then the second phase was 2010. So we have analyzed so far 52 of these homes with two visits. And what we find, again, with a quarter of the samples done, we don't see a significant decrease in the penta and the deca-BDEs, but we do see some decrease in the octa-BDEs in the dust.

So, at this point, we speculate could these reflect different use patterns. For example, with a ban, you don't go and change your sofa or carpets immediately. But as we -- the turn around and turnover of electronics, maybe newer electronics may have less BDEs, and maybe that's what we see in the drop in the octas.

I should say now we also added in the methodology additional BFRs, so next time we'll have data on not only these PBDEs but other BFRs in the dust. We also found evidence for deca-BDE debromination, being able to see the dust and seeing all the -- deca can break down to nona and octa substituted BDEs. And we see them -- their presence.

So again, with more and more evidence from other researchers as well, that deca-BDE is not as thought or has portrayed to be that it's indestructible and doesn't breakdown. It does breakdown.

And Todd Whitehead from UC Berkeley did his dissertation in our lab for this project is presenting and has presented this material in conferences.

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DR. PETREAS: And another benefit is that what we learned from this study and we're learning, we will apply with the firehouse dust, because we did collect 20 firehouses -- dust from 20 firehouses. And work is in progress to measure PBDEs, PAHs, PCBEs and some of the new BFRs in the firehouse dust.

So these were our successes and how we can help the Program, but we have many challenges. And I guess we were naive, I was naive. We thought it would be much easier and it's not.

So separate analysis are needed for separate analytical groups. Even with the persistent organics, again we take the same aliquot of small volume of serum. We can extract it, but then we need different instrument and different runs. One is to run the PCBs with the pesticides, a second different run for the PBDEs, another one for the BFRs and who knows out of our to do list for other may require more. So we have -- it takes more time.

Also, we have very, very limited equipment available to us. We only have one high resolution mass spectrometer for all the persistent organics, and the future analytes that will use this instrument.

We have one LC-MS/MS for the perfluorinated. And this has to be dedicated, because we don't want to have

contamination with the Teflon containing machines. And we have the second, the newest, LC-MS/MS that we are -- we'll be using for the phenols and hydroxy-metabolites and start to build more capacity and capabilities for the other analytes. So this is a big challenge.

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DR. PETREAS: Even bigger challenge is our staff. In DTSC, we have in the biomonitoring section, we have 40 percent vacancy rate. So out of the 10 staff, four, including the supervisor, are vacant. In addition, out of the six filled positions, both of our two biomonitoring funded staff are on leave. So essentially this year, out of two of them, we get less than one person year work.

My last bullet, we have uncertainty in APHL fellow. This will be the third year having this wonderful fellowship. And she's leaving. And we just found out yesterday that we won't get another fellow. Even though, they're very happy with us. There's so much demand now, and I can understand how they want to spread their support to other states with biomonitoring. So we're really hurting with staff shortages.

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DR. PETREAS: And as Dr. Quint had asked before, what's happening with the vacancies, our Department has been very, very not open to any freeze exemptions so far.

So basically, it's how do we balance priorities? Should we do method development or analyze samples? Given that we have so limited staff, and given that we have so limited -- it's a bottleneck with the instruments. You either have a person work on the method development, which is kind of uncertain, how long would it take, or you stop them and you have them process samples. So we have to balance and we're not always -- you know, our guesses are not always the best.

And again, just to differentiate and say we are committed to the Biomonitoring Program, but DTSC has other work for us, so we may have capabilities and capacity for work for DTSC funded projects, but not really available for this Program. So we try to do our best.

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DR. PETREAS: And this is our staff. You saw them already. And to the left are our DTSC staff, to the far right are the CDC staff and the APHL fellow and the middle are our grant supported staff. But we're all very dedicated and, you know, hopefully we'll have some breakthroughs with staff vacancies and can be more productive and present more to you in November.

So if you have any questions.

CHAIRPERSON LUDERER: Thank you very much. And very impressive to see all the new methods development for

the brominated flame retardants. We're a little bit behind schedule, but are there any quick questions from Panel members before we move on to public comments and then we'll have time for Panel discussion afterwards again?

Dr. Bradman.

PANEL MEMBER BRADMAN: I just had one quick comment, and maybe there's some discussion to follow up this. The list of chemicals where you had no capabilities yet, and there were kind of competing demands on the instrument and challenges for different classes, different methods, it underscores two things. Maybe we need to do some prioritizing within that list to -- maybe that would help, you know, the strategy to define, you know, which compounds to do first and which we have the capability to do.

It also kind of reminds me that for many of the chemicals that are out in commercial use, we don't have methods to measure them. And that's kind of a larger issue that's a challenge for the Program, but it seems that there should be some system out there when a chemical is going out in the market that we have the capacity to at least measure if people are being exposed to it.

DR. PETREAS: Is that a question for me or just a comment?

PANEL MEMBER BRADMAN: That's a comment.

CHAIRPERSON LUDERER: Are there any other clarifying questions?

Dr. Quint.

PANEL MEMBER QUINT: Not a clarifying question. I just want to say I really appreciate the level of detail that -- and that you are -- that all of you are working at in order to make sure of, you know, sample preservation and to research all of those things. As a former laboratorian, I can really appreciate the importance of it, and how helpful it will be in the long run to take the time to really explore all of these different laboratory methods.

And, you know, I just want to thank you for doing that, in spite of having such a reduced staff to work with. It's very, very impressive.

CHAIRPERSON LUDERER: Do we have any public comment?

MS. DUNN: There are none through Email, but I don't know in the room. I can't see.

CHAIRPERSON LUDERER: Any in the room?

No?

Okay. Then we have a few minutes for more Panel discussion.

Dr. Solomon.

PANEL MEMBER SOLOMON: It seems like I heard maybe three different ways that the Panel might potentially be helpful here, but I'd love Dr. Petreas' sense of those.

One is, there seemed to be a question about whether to include some of the brominated flame retardants for which methods have been developed, but which would slow down the biomonitoring a bit if they were included, whether those should be included at this point. I know my opinion I think I would come down on the side of saying, yes, if you've got the methods, yeah, these are priority chemicals and we would love to see them included, even if it would slow down the analysis of the samples. But I'd be curious what other members of the Panel think.

And then I completely agree with what Dr. Bradman said, and perhaps in the discussion later today, we're talking about priority setting or should we talk now about maybe some strategies for setting priorities within the flame retardants that have -- for which there aren't methods yet, because I think that might make a lot of sense. It's a long list, and it seems crazy for the lab to have to develop methods for each one of those if some of them are a lot more important than others.

And so I'd love to be of help there. And then the final issue is that perhaps the Panel might be able to

help, to some degree, with, you know, encouraging DTSC to fill those, you know, or at least try to fill those vacancies if they can get exemptions.

CHAIRPERSON LUDERER: Any other Panel comments?

Dr. Bradman.

PANEL MEMBER BRADMAN: I just had a follow-up. And I agree with Dr. Solomon that there might be a way we can be helpful in setting priorities among those flame retardants where there is no methods.

Also, early on in the Panel discussions some years ago, this came up around diesel exhaust, and whether there could be a request for industry to actually help develop methods. And I wonder if this might be a situation where if there was a compound that we felt was important for potential exposure for toxicological reasons we could ask for some outside help, essentially, to move that process along.

And maybe that's just a point to raise for discussion among the Panel.

CHAIRPERSON LUDERER: Any others?

Dr. Quint.

PANEL MEMBER QUINT: Yes. Julia Quint.

I just have a question. When we're deciding or trying to make a decision between methods development, as Dr. Solomon mentioned, if the method is there, you know,

she thinks it's important to actually pursue it, versus sample analysis. Because we have several projects like the MIEEP project where, you know, some samples have been analyzed, and then others have -- you know, we've analyzed for certain things, but then others haven't.

And I think -- you know, I'm also supportive of if the method exists and it's an important analyte, trying to find a way to pursue it. But I wouldn't want to holdup the results from some of these studies that we have in progress, because it really is important for us to have completed studies, to the extent that we can, to show what we've accomplished in the Program.

We have haven't been able, as we know, to do the larger representative -- you know, the larger sample. So these smaller studies have been extremely valuable. And getting through some of them to completion, I think, is going to be very important to show how, you know, much this Program has accomplished and the importance of the accomplishment. So I would like to hear a little bit more, if we decide to advise you, one way or the other, to hear more about -- a little bit more detail about what that choice would mean, in terms of completing some of the studies like FOX and MIEEP, and those sorts of things.

And to weigh that, in terms of pursuing future studies, you know, another study of firefighters or

something like that. But I think just completing the analysis so we can get a picture of what we have in the smaller studies is going to be very critical.

And then -- so that's sort of a statement, but then the next question I have is I notice that with the environmental phenols, that there is some -- that both labs are measuring certain ones, like, I think, BPA and triclosan are being measured both in the CDPH lab and in the DTSC lab. And I'm wondering if they're being measured in different media, you know, one blood and one urine or what that's all about.

DR. PETREAS: Yes, DPH handles the urine and the CDC methods are in urine.

PANEL MEMBER QUINT: Okay.

DR. PETREAS: The levels are higher in urine. We're doing the blood, because we were -- when we're doing the tetrabromobisphenol A, we could see bisphenol A. So it's hard to include too, because in many studies we have archived blood. We don't have archived serum -- archived urine.

So there are many people who would like to see if they can measure BPA in their archived serum. So that's one advantage of -- and it was something that came along as we did the tetrabromobisphenol A.

CHAIRPERSON LUDERER: Actually, I have another

question for you before you sit down.

Related to the -- I was really intrigued when you were talking about these selected brominated flame retardants that you've now developed methods for. And you mentioned that you so far haven't seen them in any human blood samples, but that you do see them in -- or they have been described in environmental media, you know, raising the question of are they not absorbed or is that they're Rapidly metabolizing, so you're risk measuring the wrong thing and measuring the parent compound.

And I was wondering what the blood samples, you know, were that you had measured them in so far? And also kind of just thinking about whether there have been any animal studies that have looked at the metabolism of any of these compounds or whether that might be an area for possible collaboration, you know, with researchers to try to look at, you know, whether these compounds are taken up and what the metabolism might be.

DR. PETREAS: Yeah. I can't speak for all the compounds, but some animal data may exist, but doses are very different. I know there are reports and publications for environmental media, sediments, marine animals may have it, dust. And up to the recent brominated flame retardant conference in Boston where staff went and that's where you find the latest thing in the corridor about

someone who's struggling with that, nobody has reported these compounds in blood. So that's why we stopped and said, if it's not just our problem, maybe they're not there. But it could still be our problem. So I'm not saying for sure. So we're still trying to make sure that we don't overdo something.

CHAIRPERSON LUDERER: Maybe just one quick follow-up question. Were these blood samples that you've used so far recent or archived?

DR. PETREAS: Yeah. These are from our -- nothing from MIEEP or FOX yet, but these are from the pilot for the teacher's study, some previous pilot data we have. Some other occupational groups we have done. So we have about a hundred or so samples. We also have blood bank blood that we see and we don't see.

CHAIRPERSON LUDERER: Any other comments?

All right. This is just about the time that we -- Sara

MS. HOOVER: I just wanted to respond to Dr. Solomon's question about prioritizing within the list. Obviously, we don't have time right now, but I have two suggestions. One would be if you wanted to have a preliminary discussion, I'm guessing we might have time, you know, at the end. We have, depending on how many comments we get for the open public comment period, we

might have a little time to take that up then if you wanted to give some initial discussion. We could also bring it back as an item at another meeting.

CHAIRPERSON LUDERER: All right. Thank you very much.

If we don't have anymore comments at the moment, we have -- the next item on our agenda was lunch. And so we had scheduled an hour for lunch. It's right now by the clock in the back of the room, I see is different than the one on the side. But we'll say in one hour, so that would be one o'clock we'll reconvene. And just I think Carol Monahan-Cummings had a reminder for us.

CHIEF COUNSEL MONAHAN-CUMMINGS: Yes. It's not nearly as applicable to this group as it may be to others. But generally speaking, you're not supposed to talk about items that are on the agenda that you are going to be opining on outside of the room. So if you have discussion at lunch please don't discuss items that are on the agenda for this afternoon.

Thank you.

(Thereupon a lunch break was taken.)

AFTERNOON SESSION

CHAIRPERSON LUDERER: Okay. It looks like most people are here, so I'd like to call the meeting back to order. And I want to welcome you all back from lunch and introduce our first speaker, who is going to be Dr. Gail Krowech, who is a staff toxicologist with OEHHA. And she's going to provide an update on chemical selection activities and present the revised greening approach possible candidates to consider for designation.

Dr. Krowech.

(Thereupon an overhead presentation was Presented as follows.)

DR. KROWECH: Good afternoon. So the purpose of this agenda item is to update the Panel on chemical selection activities, to update the Panel on the screening tool that we've been working on for potential designated chemicals, and we'll review -- I'll review the Panel's feedback on the draft screening tool that we presented in March and present a revised screening table illustrated using some organotins. And finally we want to obtain the Panel's input and recommendations.

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DR. KROWECH: This is a good opportunity to introduce two students, Bo Hu and Eileen Leung, who are working with us this summer on chemical selection

activities. And they did a lot of the important work gathering information for this presentation.

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DR. KROWECH: So the current chemical selection activities are both screening and preparing the document. We are screening potential designated chemicals: Organotins, which I'm going to talk about further a little later, pesticides from the California Department of Pesticide Regulation's top 100 pesticide list, and emerging drinking water disinfection byproducts.

We're also preparing a document on non-halogenated aromatic organophosphate flame retardants as potential designated chemicals.

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DR. KROWECH: So to discuss this screening table, this is the table that I presented at the last meeting in March. And we received a lot of Panel feedback about it. The main feedback was that production volume can be a misleading screening tool. Low volume chemicals can have a significant toxicity -- can have significant toxicity concern, and production volumes can change rapidly once the chemical gets onto the market.

Also, the Panel commented that a check mark to indicate toxicity is not sufficient, and that we should include some indication of toxicity concern and the extent

of information available.

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DR. KROWECH: The Panel wanted us to broaden categories on persistence and bioaccumulation to be sure to include when a chemical is very persistent or very bioaccumulative, and not to forget about chemicals that might not be persistent, but might -- we might be exposed to continuously, so they would be pseudo-persistent.

The Panel suggested adding more components to the screen - for example, likely routes of exposure, types and numbers of products, additional physical chemical properties and reference doses.

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DR. KROWECH: So taking all of those comments and suggestions into account, we revised the screen tool and made several changes. One change that we decided to make is to add a new category, "Reason for Concern". And this allows us more flexibility as to why we're screening a chemical.

And so some examples might be high import/production volume or indications of toxicity, very bioaccumulative or very persistent chemical, potential for exposure or a substitute coming on the market.

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DR. KROWECH: We also decided to expand the

toxicity information. So instead of the check mark, we're going to have a descriptive phrase that will really be dependent on the chemical. So it could be something like no information found, multiple positive studies, suggestive in vitro data, or structurally similar to a known toxicant. And if we have information, we'll include the toxicity endpoints.

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DR. KROWECH: So to try out this revised screening tool, we started to screen organotins. This category includes butyltins, methyltins, octyltins, phenyltins. For this example, we're just going to look at a subset of butyltins, dibutyl, and tributyltins.

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DR. KROWECH: This is a section of the table that includes the reason for concern and use information. And I just want to tell you that what I'm going to be showing are sections are the screening table. What we envision in the future is having the entire table available in a handout. But for now, I'm going to show it in pieces.

So this has the reason of concern category. For dibutyltins it's been found to be a developmental toxicant, and there's exposure from consumer products.

For tributyltins, tributyltins is an endocrine disruptor and a very persistent and very bioaccumulative

chemical. We retained the type of use compound type of use category as last time. And we also added a products applications category in response to Panel comments.

And so since dibutyltin is used as a PVC stabilizer, it's found in many PVC products in flooring and hand bags, also PVC water pipes, wallpaper, wine corks.

Tributyltins, their primary use had been in anti-fouling paint. That has been severely restricted. And in 2008, the U.S. EPA restricted a number of other uses by denying registration eligibility. Some uses that are still eligible for -- some uses which still continue are used in building materials, some consumer products, such as use in foam and fiberfill is fine, rubber mats, paper. And tributyltins are also used in livestock facilities.

In terms of the production volume, this is the production volume reported in 2006, so we have no idea what it is today, but what was reported then varied by the particular chemical. The highest was 1 to 10 million pounds for each of them.

For dibutyltins we found 16 separate dibutyltins compounds that reported production volume to U.S. EPA. And four of those had production volume at 1 to 10 million pounds.

For the tributyltins, we found three chemicals that reported production volume to U.S. EPA, and two of those had reported at 1 to 10 million pounds.

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DR. KROWECH: So this section is persistence, bioaccumulation, and other chemical properties. So what's changed here from the previous table is now we're going to be sure to note if a chemical is very persistent or very bioaccumulative. And we're including vapor pressure and water solubility.

I've put in several dibutyltins and tributyltins just to give you the idea -- the flavor of some examples. What's in blue text is an estimated value. And one of the challenges in looking at a class of compounds is the question of how many do you really need to go through to get a sense of the properties of the particular come -- particular class.

The vP and vB in bold are summary conclusions in a report for -- prepared for the EU. So if we're looking at a class of compounds, this might be one way of handling that question, looking at conclusions from reports from different bodies.

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DR. KROWECH: And as I mentioned before, we expanded the toxicity section, so we have the descriptor

and endpoints. And in both cases, there are multiple studies. There's a lot of information. I mentioned for dibutyltins, neurotoxicity, and for tributyltins, endocrine disruption. Each of them is also an immunotoxicant. And tributyltins are also developmental toxicants. And there's been a lot of new work talking about looking at tributyltin as an obesogenic compound.

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DR. KROWECH: This section on environmental and biota samples and biomonitoring studies hasn't changed at all from the previous table. I just want to point out a few parts of this or a few items on it.

One, is the house dust, one study looked -- was a New York study and looked at organotins and found very high levels of dibutyltins and levels of tributyltins. The levels of butyltins were markedly higher than the tributyltins. And also we decided to put food in this category. We weren't sure where to put it. But in this case, it was important, so its exposure is particularly from fish and shell fish. So we put it here. In the biota samples it's also listed, and you can -- basically, fish from all over the world have been contaminated by tributyltins and dibutyltins.

I wanted to mention one other thing about the house dust, which I skipped over, which was this was a New

York study. There have been several house dust studies in Europe. And the levels in the New York study were markedly higher than the European studies.

Also, in terms of the biota, there's a study on the California sea otter, which I thought was interesting for us. And again, that -- the levels in the California sea otter were higher -- the sea otters found off the coast of California -- or on the coast of California were higher than other locations where they looked at sea otters, including Washington State and Alaska.

The authors of this paper were able to do a time trend and look at levels between 1992 and 2002. And they had gone down slowly, but significantly. They also concluded that there was ongoing exposure to tributyltin though.

In terms of human biomonitoring studies, there are very few. There is one study in Michigan that found dibutyltin in 80 percent of individuals tested, and tributyltin in 70 percent of individuals. It was in the parts per billion range.

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DR. KROWECH: There were some challenges then with this screening tool, as we've just done it, is the limited information that might be out of date. And the production volume is just one example of that.

Certain type of information is not included in the screen. And we could -- I mean, we've added more. We could continue, but we're trying to keep it as -- filled with enough information, but to keep it as a screen. So that seems to be hard to decide where to limit it.

And then there are -- with a screen, it's difficult to indicate complexities and uncertainties. And with a class of compounds, that's one obvious way, but I'll give you a couple other examples.

One is that tributyltin is a contaminant of tetrabutyltin. Commercial tetrabutyltin contains about 15 to 30 percent tributyltin. So tetrabutyltin is used to produce the other butyltins, mono and dibutyltin, which are used as stabilizers for PVC production.

So you get a lot of exposure where you can't put things in neat compartments. And another factor is that dibutyltin is a metabolite of tributyltin, so it's hard to know where things are coming from.

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DR. KROWECH: So given that, we have questions that we want to ask the Panel about the screening approach and about the organotins. One is what are the highest priority categories, because we could keep expanding this. We kind of would like to get a definite idea of what we really need to be doing. And how much detail is needed in

the screening table?

For instance, when I showed -- you know, I put blood when I showed the biomonitoring studies, but what would be important to know for screening as in location, date, frequency of detection, levels, number and sample? It's hard to know what is really needed for a screening.

And then how far should we go in researching certain questions? There are several papers that I found in trying the screen this that showed tributyltin was found in biosolids. And so the question is like how far do you go looking at this to see is this important? And, you know, I'm just sort of wondering for screening purposes what we really should be focusing on.

So we have a proposal, which is to use a flexible, iterative approach, depending on the specific chemicals and research questions, so that for some chemicals we might have more categories, for others we might have fewer. And we could have a process whereby we bring a screen to you and you ask further questions, which we could bring back as part of the screen for the next meeting.

And so it could be used, the screening could be used as a dialogue of where do we go with this particular chemical.

--o0o--

DR. KROWECH: And in terms of the organotins with this idea in mind, we'd like your input on should we move forward with these chemicals? And if we should, should the program develop more screening information on butyltins, more on dibutyl and tributyltins, should we include monobutyltins? Should we screen information on additional organotins, such as octyltins, which were also really high in this house dust study? Or should we develop a potential designated document on a narrow class, such as dibutyl or tributyltins, or should we develop a document on a broader class, such as butyltins?

So I'm happy to answer questions and turn it over to Dr. Luderer for discussion.

CHAIRPERSON LUDERER: Thank you very much. You've really come back and responded, I think, to a lot of Panel member comments from the last presentation.

Do Panel members have additional questions?

Dr. McKone.

PANEL MEMBER McKONE: Thank you. That was very interesting, and I do appreciate, I think all the Panel here does, of providing some of the additional information, like seeing the uses and market.

I have one real quick question, how do you get this out of liver? Did you say one of the issues was liver or was that cadaver? Human liver was one of the --

DR. KROWECH: Oh. You know, I actually looked at the study. I can't really remember right now, but I think they were biopsies. They were taking a biopsy in there.

PANEL MEMBER McKONE: All right.

DR. KROWECH: And it was in all -- dibutyl was in all samples, by the way.

PANEL MEMBER McKONE: So on some of the questions -- the other thing is the idea of the adaptive strategy is probably a really good one when you're not quite sure.

So this question of I think -- your overarching question is like, so what, right?

I mean, so we see it and what does this mean, and how do we know if it's important or not? And I think in addition to the biomonitoring, your question is are we watching something on an upswing, steady state, or a downswing, right?

And I think any information that would help understand this -- I mean, if we're -- if what we're seeing in humans is only the beginning of a rising trend, then it's probably -- even if it's relatively small relative to toxic endpoints, you'd be concerned about what the slope, what's the rate of change in time.

And given that these are persistent compounds, right, they were either persistent or very persistent in a

lot of the ranking. They can -- we can start to see a trend where they're really rising.

So I guess the things that would hope understand that, which appear to be hard to get, is the market trend. I mean, what is the production volume, and where is that going? I think with any of these substances, when there's a major new use that suddenly will rise up and whatever we have now doesn't mean anything, because it's what's going to be there. So that's one thing to try and do to get a little better handle on the market.

And then I think the other one would be to look at some of the dynamics in the environment. I mean, there are some of these mass balance models, which actually will predict the trends in the environment. And you can see how the environment looks relative to what they predict to sort of figure out this -- whether the system is stabilizing or just on the upswing.

I mean, that might -- just some suggestions off the top of my head for -- you know, the one thing that's probably easy to get, easier to get than the modeling, would be to try and look at the market trend, because that's an underlying issue. But then you can use some modeling to see whether the world looks like -- modeling combined with some of the monitoring data to see if it makes sense, of whether there's an upswing or a downswing

or a steady state world that we're seeing in the samples.

DR. KROWECH: Okay.

CHAIRPERSON LUDERER: Dr. Solomon.

PANEL MEMBER SOLOMON: Thank you. That was a very helpful presentation. And I have some questions about your questions to us.

DR. KROWECH: Good.

PANEL MEMBER SOLOMON: You ask what are the highest priority categories. SO you mean of the different rows in the table, which ones do we think are most important to fill-in as a priority? And then in terms of how much detail is needed, I guess my question back is, you know, personally I kind of like the level of detail. I sort of felt like you got it right with the organotins, but how onerous was that? Like was that a big, you know, large amount of staff time that went into doing that? Is that doable for other chemicals? Or should we -- you know, should we be having a discussion about could we, you know, get away with less?

So, you know, I just want to know if we're asking if it's doable what we were asking here?

DR. KROWECH: I think if we tried to look at it in terms of a couple of categories and try to get the details on those, that would be manageable. But again, if we had a list of pesticides, it would be, you know, more

time consuming to try to fill all of that out.

So, this -- I mean, maybe there wouldn't be enough information, so that might solve that problem. But I think with the biomonitoring studies, you know, we could fill it out. I mean, it's hard to know what it means when it just says blood or breast milk. So I agree that it's good to have information, but if we need that in all categories, it's hard to put that on the table.

So I guess do we envision this as just a continuous presentation, that would be one way of looking at it, is that they would always be presented in -- because otherwise putting all those details in a table doesn't seem really easy.

CHAIRPERSON LUDERER: You want to follow up?

PANEL MEMBER SOLOMON: Yeah just a follow-up. So like -- I mean, what I find useful about just having blood or breast milk in the table is then I know that there's at least one publication out there in which somebody has developed a method for this in that medium, and presumably has detected something. I guess if they developed the method and failed to detect anything in any samples, that would probably be worth noting.

But it -- what that just -- you know, so at that level, I think, you know, from my perspective just having blood or breast milk or urine or something in the table is

very helpful.

And, you know, I could see if we wanted to -- you know, we might, in certain circumstances, want more information or it would be useful to have a sense of, you know, the percent detects or something like that.

DR. KROWECH: Okay. I guess another question that I forgot to mention was what about negative studies? You know, if I only put the positive studies in there, you know, what about a negative study?

So, in this case, there was one negative study. And the location was very different, but I'm just, you know, trying to weigh all of this. How much do we fit into a screen? Because obviously with a document, you go into all of this.

CHAIRPERSON LUDERER: Dr. Quint.

PANEL MEMBER QUINT: Julia Quint.

I think some of this is going to -- the green light is on. Can you hear me now?

Julia Quint.

I think some of it is going to be judgment on your part, which I trust implicitly, given your experience with these things. And I think what you've presented here is -- I mean, I can look at this and tell right away whether or not I'm interested in pursuing certain things. There are some questions like when you ask about octyltin,

I would like to know more about structure activity relationships within these chemicals and whether or not, you know, having the butyls and -- or, you know, more carbons on the tin would make a difference. Those kinds of things.

But I think those are the same questions you would be curious about. And those could be captured in some sort of comment annotation on the table, as opposed -- you know, which would vary by chemicals. For pesticides, I'd be much more interested in use in California, as opposed to some of the other use data, because, as you said, it's changing and the trends that Dr. McKone talked about are going to be more important.

But, you know, the basic questions are is there a toxicity of interest, potential for exposure? I mean, some of the constants if they aren't there, I think that's helpful. But, you know, if it takes a lot of time to pursue those, I would be less interested.

But what they're in. You know, if something is in a rubber mat that's used outside versus PVC flooring that's inside, that's going to tell me something very different about potential for exposure.

So I think your iterative process, your proposal is right on the mark, in terms of using judgment. And we are going to eventually want to biomonitor. But at first

we're going to designate and then decide whether or not we can move forward in terms of methodology.

So having some of the -- I mean, if there are data as Dr. Solomon said about whether or not somebody has published something in blood or breast milk or whatever it is, that's very helpful, but it's not going to really be definitive in terms of us maybe designating it as something that we'd want to look into further.

I think not spending a lot of time on every chemical in the class, like all the different compounds, I don't think that that's warranted before we, you know, just check in on the significance of it from your initial screen.

But, you know, I think time, how much time you spend on it is really -- we don't want to use all of your time on these things, because it really is a screen.

CHAIRPERSON LUDERER: Any other comments or questions from other Panel members?

We might take public comments now and then we'll have more time for discussion after that.

Do we have any public comments?

MS. DUNN: Anyone in the audience?

I have one.

CHAIRPERSON LUDERER: Okay. We have one public comment that came in via the web. This is from --

The green light is on.

Okay, can you hear me now?

This is from Cheriel Jensen.

And the question is, "I did not see RoundUp glyphosate or POEA on the list of chemicals to be tested for. As (these) is (are) probably the most common environmental chemicals used today, why is it not on the list?"

And I'm not sure whether she's referring to maybe the designated or priority chemical list. It just says list of chemicals to be tested for.

MS. HOOVER: Everyone seems to be looking at me. Could you repeat the list of chemicals?

CHAIRPERSON LUDERER: The chemicals mentioned are RoundUp, glyphosate, or POEA.

MS. HOOVER: I guess --

CHAIRPERSON LUDERER: PFOA must be. PFOA.

MS. HOOVER: I guess the way I'll respond to that is that, I mean, I know that -- and turning to Gail -- glyphosate is in our list of things we're screening. You know, so we're aware of glyphosate. If it's PFOA, it's a perfluorinated compound, so it is -- that is on the list.

So I think we would -- Gail did you want to --

DR. KROWECH: We are screening glyphosate. And I believe that RoundUp -- that glyphosate is in RoundUp.

MS. HOOVER: Yeah. So, you know, we'll just -- we're happy to take any comments on candidates we should screen, and we'll add them to the list that we're screening.

PANEL MEMBER McKONE: Apparently, it's an inert ingredient in --

MS. HOOVER: Pull it closer to you, Tom.

PANEL MEMBER McKONE: Closer. POEA -- okay, I'm looking. Inert ingredient in RoundUp. Let's see, POEA is a surfactant or detergent arrived from animal fat. It is added to RoundUp and other herbicides to help them penetrate plants. Associated with acute and chronic effects.

Here's what it is, polyethoxylated tallowamine surfactant.

All right. So it is an element. Glyphosate and POEA are both elements of RoundUp, according to this or components of RoundUp.

MS. HOOVER: Okay. Sara Hoover again, OEHHA. So we'll include looking at that as part of the screening of pesticides that we're doing.

CHAIRPERSON LUDERER: Okay. Thank you.

So if we have no more public comments, then we have more time now for some additional Panel discussion on this topic.

PANEL MEMBER BRADMAN: Asa Bradman. I'm just wondering if maybe in addition to this tool would be if there's a benchmark dose or point of departure available by any federal or State agency, that it might be worth including that. There was, you know, some tox information on whether there were positive studies or negative studies. I know for many chemicals we don't have those references and there can be issues within that said. They provide maybe some means to compare compounds.

Also, if we have some information on use, you could, you know, take the inverse of the benchmark dose and multiply it by the use and you get someway of ranking the potential risk out there of the material. Although, of course, that doesn't account for actual exposure. But it might be another tool that would be helpful to flesh out the table.

DR. KROWECH: I just wanted to say that there was a reference dose available. I didn't include it, because -- well, first of all, because I couldn't really include everything, but it was based on immunotoxicity. And so it's older. And then now there are, you know, more concerns with endocrine disruption and developmental and neurotoxicity. So, you know, I didn't know how useful that would be.

PANEL MEMBER BRADMAN: Right. So many of these

benchmarks are going to have some limitations.

CHAIRPERSON LUDERER: I just have a clarifying question about one of your questions again, which was is your last question about the flexible iterative approach kind of instead of the screening table or are you thinking of this in addition to the screening table?

DR. KROWECH: Well, we're thinking of it more as part of the screening table, that we would bring you a table and then you might say I'd like more information on these kinds of studies, and then the next time we'd bring that table back with that, and we could maybe just discuss that information.

CHAIRPERSON LUDERER: Okay. Thank you for clarifying that. I thought that's what it was, but I wanted to make sure that I was understanding that right. And I want to just agree with what the other Panel members have said. I mean, I think that the level of detail that you have in the screening table now really does provide us with a lot of information that I think is, from my perspective, I think sufficient for us to be able to then come back in an iterative approach and ask for maybe additional information about specific compounds or specific additional details for chemicals.

Dr. Solomon.

PANEL MEMBER SOLOMON: With regard to the more

specific questions on organotins, you know, I see enough of concern in what you've provided to us today that I would be very interested in proceeding with a potential designated document.

I'm having trouble answering your question about whether to make it a more narrow class or to broaden to include all of the butyltins, and would be open to either. I don't have a good sense of what other -- you know, you mentioned octyltin. And so you may know more than we do about how -- what makes most sense.

But if these different butyltins are sort of breaking down into each other, it might make most sense to look at them as a larger group. And so I guess I'd be leaning slightly toward the broader class, unless there's some reason not to.

And in my view, one of the more important questions to answer is, you know, since some uses of tributyltins have been phased out, and there's some indication that you mentioned from some of the studies that levels may be declining in the environment, you know, I think a lot, for me, is going to be hinging on, you know, if these chemicals are sort of -- you know, if they're going away, I'm going to be less excited about, you know, putting resources into biomonitoring for them, versus if they're still very much present or maybe certain

butyltins or potentially their uses may be increasing, that will make me much more interested in putting resources in to biomonitoring them. So I think that, you know, summarizes my thoughts on the organotins.

CHAIRPERSON LUDERER: And I actually was -- I am going to agree with a lot of what Gina said. But in terms of narrow versus broader, I mean, another -- I mean even broader would be organotins obviously. And maybe -- I'm not sure if I'm remembering this correctly, but don't triphenyltin have similar obesogenic effects as tributyltin. So that may be an argument for broadening it even further.

Any other comments or questions from Panel members?

Dr. Quint.

PANEL MEMBER QUINT: Julia Quint.

You've been so great at looking at emerging chemicals that are replacements for things that have been deemed toxic. And I'm wondering if there's been any -- if you've seen anything that looks like it's replacing the tributyltin as a biocide or something that we should just keep our -- not, you know, look at in any robust manner at this point, but just keep an eye toward replacements, you know, substitute chemicals that might be just as toxic or toxic in a different way, because that's always a problem

It looks like the dibutyl is not. They're totally different uses of those two chemicals, so that's not being used in its stead, but there may be something else on the horizon that we should be paying attention to in that category.

DR. KROWECH: I haven't seen anything yet. But one thing is the EU has started to severely restrict the dibutyl. And so in 2012 there's going to be, you know, severe limits on how much there can be in certain products. So I'm not sure what it is, 0.1 percent. So there will definitely be substitutes coming on the market.

PANEL MEMBER QUINT: And that's going to affect the market here?

DR. KROWECH: Yes.

CHAIRPERSON LUDERER: Have we addressed your questions initially?

DR. KROWECH: (Nods head.)

CHAIRPERSON LUDERER: Okay. Great. Then we can move on to the next presentation. And Sara Hoover Chief of the Safer Alternatives Assessment and Biomonitoring Section of OEHHA will introduce our next speaker, who is going to be Dr. Roy Gerona.

MS. HOOVER: Okay. I just first wanted to say that the reason we're doing this item is partly because of the Panel's interest in screening unknowns, but also the

Program's interest. So we're all very interested in this concept. And Dr. Solomon had introduced me to Dr. Gerona. And I've heard him speak and was eager to bring him to the Panel so you could hear him as well.

So Dr. Gerona, I'm just going to give you a little background. Let get my glasses on.

Dr. Gerona got his Ph.D. at the University of Wisconsin, Madison in biochemistry. And he's now a post-doctoral fellow in clinical chemistry at the University of California, San Francisco in a joint program with SF General Hospital.

And his research is focused on exploring clinical applications of TOF LC-MS analysis and with a current focus on a number of projects, including developing serum test panels targeted to respond to drug overdose cases presented to emergency and trauma centers. He's also going to comment briefly on a new project he's working on in using non-targeted TOF LC-MS methods for discovering unreported or underreported environmental toxins in pregnant women.

And he's also facilitated the implementation of providing toxicological consultation and analysis to emergency toxicology cases referred to the SF Division of the Poison Control Center.

So I want to hand it over to Dr. Gerona.

(Thereupon an overhead presentation was Presented as follows.)

DR. GERONA: Good afternoon, everyone. First of all, allow me to thank Sara and Gina for inviting me over to share with you some of the exciting things that we're doing at the San Francisco General Hospital Toxicology Lab, specifically with respect to non-targeted screening of biological samples for environmental contaminants.

Unfortunately, we have just gotten -- well, fortunately probably, we have just gotten funding for this project. And so I and my collaborators are, I think, not yet ready to divulge a lot of the initial information that we're getting for this particular project.

As you might have probably noticed in the slides that I have forwarded, we have only allotted one slide for the actual project. We have some pilot data, but we would wait for the confirmation of the data that we have gotten so far before we can report it publicly. So we will be happy to come back and report to you once we have actually gotten confirmation of that data.

So what I will do this afternoon basically is to discuss the concept that is involved in this kind of novel approach for environmental screening. I think this has never been done on environmental contaminants in biological matrices. So a lot of the slides I would tell

you in advance are more geared towards the laboratory part of it.

I would be happy to address some of the questions that you might have regarding the technique once the presentation is over.

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DR. GERONA: All right. Just to give you a guide as to how my presentation will proceed this afternoon. I will first give you a very simple rationale for non-targeted analysis, why it is a very good alternative to the targeted screenings that we're all doing in environmental biomonitoring.

Then I will devote a lot of time explaining to you the basic principles involved in time-of-flight mass spectrometry, that's what TOF stands for, and how it can be used for non-targeted screening.

I will give an example of a TOF analysis of environmental pollutants as proof of principle that this has been already done in other environmental samples. And the data for this particular study has been published in the literature. It hasn't been done yet on biological matrices though. And that's what we're trying to do.

And then I have one slide on the TOF analysis of environmental toxins in biological matrices that will introduce to you the project that we are doing with Tracey

Woodruff's group at the Program for Reproductive Health and the Environment at UCSF.

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DR. GERONA: Well, so why is it beneficial to do non-targeted analysis?

As you're probably all aware of, there are more than 3,000 industrial chemicals produced and imported in this country in over one million pounds a year. However, there are roughly about 300 chemicals that are being biomonitored by targeted analysis. So what happens to the 2,700 other chemicals that are being produced?

Well, we can systematically target them for analysis by targeted analysis, but will that be practical?

Targeted analysis will always require a reference standard for a particular compound. When you develop a method, you need a reference standard. For some of this -- actually, not some, but a lot of these compounds, having the reference standard available commercially is usually next to impossible. Add to that the problem that in a lot of these environmental toxins, it's not the parent compound that you'll find in the biological matrix but the metabolite of that particular parent compound.

So looking for reference standards for this particular other compounds that are not being biomonitored yet may be, one, costly. And if you're going to

systematically analyze 2,700 or more compounds, that will be very time consuming.

So a very good alternative then is to do non-targeted screening of environmental toxins in biological matrices and then follow that up with quantification of those particular toxins that would be found at high frequency in the subjects in a particular study.

The required analytical platform for this kind of approach is time-of-flight mass spectrometer. So what is TOF mass spectrometry?

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DR. GERONA: Simply put, this is an analytical technique based on the separation of molecules according to their charge to mass ratio. And if you are only screening for compounds that has plus 1 as charged, then this is a separation based on molecular weight. This particular technique involves ionization of molecules, and then sorting them out according to their mass.

There are several types of analytical platforms that can be used for TOF mass spectrometry, based on the type of ionization technique and based on detection. The more common ones are those that require soft ionization, like electrospray ionization, and atmospheric pressure chemical ionization. That's EIS/APCI TOF-MS. There's

also a more advanced or higher upgrade of platform called QTOF-MS. Of course, everyone here might already be familiar with MALDI-TOF that's used for larger molecules like proteins. And then another upgrade to the TOF, which is very good at high resolution mass spectrometry is the OrbiTrap.

This is not a new technique. The first mass spectrometers with TOF analyzers appeared in the 1950s. I guess the main limitation as to why they have never been used for non-targeted analysis is the ability of these older generation machines to actually accurately measure masses. So the older generation ones have low resolution, and they cannot accurately measure molecular weights.

With the advent of great improvements to the resolution and high mass accuracy, it became possible for TOF-MS platforms to actually unambiguously assign molecular formula to a molecular -- measured molecular weights. And that's where this technique actually hinges on, as far as non-targeted analysis. I would discuss that a little bit in more detail in the next slides.

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DR. GERONA: In order to increase the level of resolution for most of this TOF-MS machine, they're usually used in tandem with chromatography. That's either LC or GC.

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DR. GERONA: So in simple terms, this is what is actually involved in this particular analysis. So normally, because every machine is linked to an HPLC or GC, the eluent that's coming out of an LC or a GC machine are then fed on to the first part of the machine, which basically generates the ions.

Okay. Those ions are then fed onto a mass analyzer, which separates those particular ions according to their masses. And then it's detected using an ion detector, which is usually using scintillation counting as its basic principle. What you'll get as a readout is the mass spectra of a particular known.

As you can see there, it's basically just the measured molecular weight versus the abundance of that particularly ion.

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DR. GERONA: So what's the basic principle for time-of-flight mass spectrometry? It starts with the ionization of the molecules. Once the molecules are ionized, it's then fed onto what's called the time of flight tube.

Oh, sorry.

So this is the time of flight tube where the separation happens. And the principle is simple, all

molecules of differing sizes are given the same voltage jolt, so then they are accelerated by the same kinetic energy. So if each ion with different size are accelerated by the same kinetic energy, the Velocity by which they would travel in the drift tube will then depend on their mass. The lighter the ion, the faster that ion would travel. The heavier the ion, the slower the ion would travel.

So this technique actually hinges on measuring the time-of-flight of the ions, right. And the time of flight is proportional to its mass by charge ratio.

So as I've said earlier, the utility of this machine hinges on the high mass accuracy or its ability to measure molecular weight in a high mass accuracy, that is sub 2 ppm level for most of the modern platforms that we have. And this allows unambiguous assignment of formula to measured molecular weights. I will discuss what that sub 2 ppm accuracy actually means when it comes to actual molecular weight.

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DR. GERONA: So this is another simplification of the principle involved in TOF-MS. So you have a set of molecules of different sizes. If you give them the same kinetic energy, as you can see the lighter ion travels faster and hits the detector first. So it's the

time-of-flight of each of these ions that actually are measured.

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DR. GERONA: So I mentioned earlier that the accuracy of the measurement is based on what's called the mass error, right? So you would hear people in the TOF-MS community ask you about how many ppms is your measurement accurate?

Well, mass error is basically a quantification of the difference between the measured mass, okay, by the instrument and the theoretical mass of a particular compound.

Here I have, as an example, 2 ppm. So what does 2 ppm mean? Well, because as you can see in the equation, molecular weight is in the denominator of this equation. Two ppm would depend on the molecular weight of the compound you're measuring. For a 100 atomic mass unit, that means that the accuracy of the measurement is up to the 0.0002 amu.

So most of the organic compounds that we see in the environment are actually in this particular range. So it's fair to say for most MS, TOF-MS platform that the accuracy is up to the fourth decimal place.

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DR. GERONA: What's the importance of that as far

as assignment of molecular formula to the measured mass? Here's an example of isobaric compounds. Isobaric compounds are compounds with the same nominal mass. You can see they are both 285.

If you're using ordinary LC-MS/MS, the Q1 scan or the scan of the parent ion here will not allow you to distinguish between morphine and pentazocine. They're both 285, and the resolution is only up until about that.

But the ability of TOF-MS to actually measure up to the fourth decimal point with differentiate two molecules. Although, they have the same nominal mass. One is measured at 285.1365, and the other one will be measured 285.2093.

I have here another example. If say you have a molecular weight that was measured by a machine at 285.1365, if the resolution is at nominal mass, okay, like what the Q1 of LC-MS/MS -- most LC-MS/MS have, there will be potentially hundreds of formula that will have -- will share the same molecular weight.

At 10 ppm accuracy, assuming that you have only carbon, hydrogen, oxygen, and nitrogen, that's down to five possible formula. And as you can see here at 3 ppm accuracy, only one possible molecular formula can be assigned to that particular mass. So the principle is simple.

I mentioned that most platforms can actually achieve sub 2 ppm accuracy.

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DR. GERONA: What is the generic protocol for these kinds of analysis?

The first step in this kinds of analysis is to actually measure a full scan mass spectra of the sample obtained. So for targeted analysis, you usually measure particular masses. All right, you have transition that you measure.

In this particular technique, you have a full scan mass spectra of everything in your sample. Then an algorithm that usually comes with the instrument will generate the best fit -- sorry, I have gone ahead of my slide.

So an algorithm generates all the masses measured with a specific retention time of that particular mass that was measured. Then another algorithm that usually comes with the machine will assign the best fit formula to that particular mass.

Now, to give more information to what you have as molecular formula, you need to be able to identify what that formula represents. And this is where the targeted part of the non-targeted analysis comes in. In order to generate a compound that would fit that formula, you need

to create a database that would have the formula of all the compounds that are possible that you're interested in.

Say, for example, if you have environmental toxins, you can have a list of 3,000 environmental toxins, even without reference standards, just a listing of the 3,000 environmental toxins, and their formula. The platform will compute the exact mass of that. So what the machine will do is actually to fit what particular environmental toxin would have that formula that it's measuring.

Now, does that give you a confirmation right there?

No. To confirm your results, this is where you would actually need a reference standard for those high frequency chemicals that you then have measured in your non-targeted analysis.

So basically, this will guide your analysis. It's not totally non-targeted, but it at least guides you to where -- which particular compounds to look, because those are potentially in your samples.

What's also very good in this particular approach is that as you can see here, step 1 is full scan mass spectra. Say, for example, now in 2011 my environmental toxin database has only 3,000 chemicals. In 2015, for example, I've add 3,000 more to my database. Because I

have actually collected full scan mass spectra in 2011, in 2015, if I have a larger database, I can just look back at the data without running the sample again that I've generated in 2011 and ask was that compound in the sample in 2011?

So it gives you so much power as to how much data you can actually mine from the first -- from the first step in this particular process.

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DR. GERONA: So here's a demonstration of what you can do. So the first set of information that this particular machine provides is a paired retention time and mass, and that -- this is a particular sample that we obtained for a patient that is in polypharmacy, and we're trying -- this was referred actually to us by the Poison Control Center. And we're trying to figure out what particular drugs is this patient -- has this patient taken.

So this is just a collection of the masses and the retention time that has been measured in the sample.

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DR. GERONA: In order to generate more information in this collection of retention time and masses, we generated the best fit formula to the mass. So the mass column here, these are the best fit formula.

And then we run a database -- we have a forensics database that contains 7,000 pharmaceuticals and pesticides.

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DR. GERONA: And these are the matches that we obtained for this particular patient. All right. So this patient is obviously in polypharmacy. They have methadone, levamisole, oxycodone.

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DR. GERONA: Sometimes in the literature, you will see QTOF instead of TOF. Well, what is that?

I've already mentioned that this is an upgrade of the TOF. QTOF refers to quadrupole time-of-flat mass spectrometry. And what it simply means is that there is an addition of a quadrupole in front of the TOF analyzer.

The quadrupole actually allows you to select a particular mass, so that if you're interested in a single molecule, okay, you can fragment that molecule and also measure the exact mass of its daughter ions. What's the utility of this particular ability to measure accurate masses of both the parent and the daughter ion?

Well, it allows structure elucidation of unknowns. Say, for example, you have obtained a compound that's high frequency, but there's no reference standard, another way of doing it is to do structure elucidation.

And QTOF has the ability to do that as well.

So as I told you, this is not a novel approach as far as environmental pollutant screening is concerned. The first publication came out of Netherlands where they actually used the approach in wastewater. And so they have tried identifying contaminants in this particular environmental sample.

The approach has also been applied to food -- sorry -- the food and pharmaceuticals. And lately given higher grade mass spectrometers, like OrbiTrap mass spectrometry has also been used.

How am I doing on time?

I have five minutes.

Okay.

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DR. GERONA: All right. So just to give you an example of a study that actually used this in identifying particular contaminants, this was a study that was done in Spain by the group of Bueno et al.

So what they did in this particular study is they tried collecting samples from sewage treatment plants and screened them for -- they have a very small library here. They have only 56 pharmaceuticals, pesticides, and I think disinfectants. And, you know, it's concerning to see some of the compounds in all this. I think they have about 20

samples. And these are the positive hits that they have in those 20 samples.

So you can see caffeine. That's not really concerning, but you can see ibuprofen there, beta blocker like atenolol, and even codeine in these effluents.

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DR. GERONA: And here's an example of identifying an unknown. In this particular study, they have found dipyrone, which is an antidiuretic. And in previous studies, metabolites of dipyrone has been identified in river waters. They have included in their library one of the metabolites of dipyrone. I think it's methylaminoantipyrine, which they have found in the sewage treatment plant waters to be very high in levels.

Then in their unknowns, they also have found a persistent molecular weight. This molecular weight 246.1237 present in a lot of samples.

All right. They did run an unknown targeted analysis of this. And what they found out is that this particular molecular weight actually coincides with the mass of 4-AAA is another metabolite of dipyrone. Okay.

So I don't think they have a reference standard for this initially, so what they did is they do have a QTOF. They tried to fragment the ion. And what they have found out is that there are two fragment ions here, which

are the expected ions, of this particular unknown is 4-AAA. And so that's kind of like what the process will be if you don't have a reference standard. You can run exact mass analysis of the daughter ions and see if it will fit what you have.

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DR. GERONA: And finally, this is the study that we're doing with Tracey Woodruff and Ami Zota. I've already set a rationale for this. There are no non-targeted analysis of environmental toxins in biological samples that has been reported so far.

The objective of the study would be to use unbiased interrogation methods to identify previously unmeasured environmental chemicals in the serum of pregnant women.

I'm allowed to say a few things. So here what we will do is we will develop a chemical database for environmental toxins. So that will be our basis for the non-targeted analysis for giving some identity to the molecular formula. We would use about 20 retrospective samples. These are ethnically diverse. We will then look at high frequency environmental toxins that has not been reported yet. We would rank them and the top 10 to 15 chemicals we would develop a targeted analysis for them, so that we can quantify their levels in these women.

So as I've said, the method is TOF LC-MS. And the funding source for this study is through the Passport Foundation.

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DR. GERONA: I'd like to thank my advisor, Dr. Alan Wu, who has made all these studies possible and my collaborators at PRHE.

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DR. GERONA: And I'd like to end with showing you some of the platforms -- oh, what have I done? -- showing you some of the platforms. I need to show the platforms. So these are some of the platforms available for this kind of study. We have this already. This is what we did for a pilot study. I was going to say that we also did some pilot study.

And unfortunately, I cannot reveal to you some of those results. But we have already found at least three chemicals that hasn't been reported yet. It's not confirmed yet, but there are three chemicals that we're finding out in our pilot study that has not been biomonitored yet. So we find that really very interesting.

We have just gotten an OrbiTrap, and it's being installed in our laboratory this month. And we're expecting a QTOF AB SCIEX 5600, which probably will be the

workhorse for this particular study. The OrbiTrap is good to have just in case we have difficult unknowns where we cannot find reference standards for, because this has a very high resolution.

So with these kinds of platforms, one should be able to do environmental biomonitoring using a non-targeted approach, which I hope people would be interested in, because there's really, I think, a lot of information that this can provide us that we don't have now, which would otherwise be very difficult to do if you're doing targeted analysis.

Thanks for your time and I'd be happy to take questions now. And I'll turn the floor over to Dr. Luderer for the Panel discussion.

CHAIRPERSON LUDERER: Thank you very much, Dr. Gerona. That was very interesting and very exciting and something the Panel has been talking about for some time.

Any questions or comments from Panel members?

PANEL MEMBER BRADMAN: I have to think about this.

(Laughter.)

CHAIRPERSON LUDERER: Are there -- I'll just ask a question. Are there any particular challenges that you think that there might be with matrices like, well, say blood for example versus some of the other matrices that

have already been published on?

DR. GERONA: Sure. Sure.

CHAIRPERSON LUDERER: I mean, sewage treatment effluent sounds pretty complex.

(Laughter.)

DR. GERONA: Yeah. I guess my colleagues in the laboratories here would agree with me that biological matrices are far more complicated than water.

We have some experience in developing a method for BPA, and its conjugates. And, you know, we do -- every now and then, we find some particular samples very challenging to measure. And so I guess to answer that question, we have, I think, enough tools in the laboratory to do clean-up process for a lot of these compounds.

Also, we are not going to -- in this particular study, we're not going to use only one approach in sample extraction. So we're actually -- when we are developing the method, we are developing a method where we do simple protein precipitation alone, solid phase extraction, And liquid extraction. And the idea is to capture as much environmental toxin as possible.

That's also the reason why we're not only using ESI as our ion source, because obviously ESI is very good for very polar compounds, but you would be missing the more non-polar ones. And so we have actually put in two

different ionization sources for this particular study.

So we are aware of the complications in the biological matrix. And our approach to that is to use different sample preps and different sample clean-ups to maximize the amount of signals that we'll get.

Of course, the downside to that is that the analysis of your results will be a little more complicated. And I guess we haven't sorted out all the analysis so far, because our data is -- we haven't gotten a lot of data yet to address that particular issue.

Does that answer your question?

CHAIRPERSON LUDERER: (Nods head.)

Dr. Solomon.

PANEL MEMBER SOLOMON: Can you -- fantastic presentation, by the way. Thank you.

Can you tell us a little bit more about the reference libraries and the limitations that might exist there. And I understand some of these reference libraries are proprietary, that there are some that are being developed that may be public. I'm curious how many chemicals are in these different libraries to compare against.

DR. GERONA: Sure. So we were surprised when we were in the initial stages of developing the chemical library. And we haven't finished yet in this particular

activity. But there is really no open source out there that would give you a list of all the chemicals and their respective chemical formula.

A lot of the sources would say that they're open source, but you can do individual queries. What we need for the chemical database is a simple listing of the chemical name and the chemical formula. We don't even need the structural formula. We need the chemical formula, because the software of the machine would determine or will calculate for you the exact mass.

So then we said, okay, so this is our first challenge. How are we going to put together all of these environmental toxins. So far, we've referred to NHANES. Agilent has a forensic database that includes at least 500 pesticides and herbicides, insecticides. So we've gotten that.

We have used results of biomonitoring studies, which I know is not target -- it's a result of a targeted analysis. But we've also used the high production volume database by the EPA HPV program.

There is this MDI biolab that has a listing of 100,000 environmental toxins. And so we've looked at the chemicals also. And we have, interns and post-docs who are assiduously searching for the formula of each of these compounds. So right now we have about 700 in our

database, and we're continuously adding compounds in our database.

Our goal is to at least have a 1,500. There's other limitations. Polyaromatic hydrocarbons, for example, will not ionize in the sources that we have.

So in that sense, we won't be able to look for those, unless my boss would agree to buy another ion source that we would -- we might be able to use for this particular study. But right now I'm not banking on it.

So there are limitations also as to the types of compounds, those that are very difficult to ionize. It might be in our chemical database, but we already know that we won't be able to find them, because we will not be able to ionize them using our method.

Another limitation of the TOF right now or the QTOF is in quantification. And that's the reason why, if you've noticed in the approach that we will be doing, we will not be relying on the TOF for the quantification. We will actually rely on LC-MS/MS for quantification. So it will be a tandem technique, right. So we will do qualitative analysis using the TOF, because that's what it's good for.

Once we've identified high ranking chemicals, those with high frequency, we will then try to find reference standards for those, and develop a quantitative

method using LC-MS/MS.

The problem with the TOFs right now is it's ability to -- its limitation in the linear dynamic range that it can measure for a given analyte, so it's very, very limited.

It's in the hundreds as opposed to 10 to the cube or 10 to 4th. What I'm talking about here is what is that range of concentration where your measurement is still linear. Right. Can you go from 0.1 ppb to 1 ppt, parts per thousand. In some platforms, that can be achieved. In the TOF, from our experience, we haven't achieved more than 10 to third. So that's a limitation also. And that's why we're still relying on LC-MS/MS for quantification.

CHAIRPERSON LUDERER: Dr. Quint.

PANEL MEMBER QUINT: Julia Quint. Thank you. Not only was your presentation elegant, but you did such a good job of explaining something that potentially could have been very complicated, so I appreciate that.

DR. GERONA: Thanks.

PANEL MEMBER QUINT: I think the possibilities with this seem almost limitless. And I think also it raises, because there's such a great potential to get so much information, this could also be a challenge, I think, in terms of, you know, biomonitoring, because we're

struggling now with what -- how do we present results to people and how do you really explain what they mean and all of that. So this adds to that, not that that's not a challenge we can't meet, but it just is another challenge.

But I also, I was wondering, I mean, you know, in this process too, you can detect potentially almost everything in a sample in drugs and, you know, things that you may not be looking for, in terms of a certain -- you know, if you're looking for environmental contaminants. And is there an ability, say, if you were measuring contaminants or analytes in the -- for pregnant women and their infants, is there a way for you -- do you automatically just decide what you're going to analyze or do you have this, you know, commitment to just disclose everything, because we're taking an a narrow view in biomonitoring that we're looking for certain environmental contaminants. And from that we're making -- we're doing that so we can look at, you know, some of the implications of our policies around environmental contamination.

But in this type of analysis, I mean, you can have somebody who is also taking ibuprofen or taking, you know, drugs or whatever. And I'm just wondering about the sort of ethical conundrum that that might present, in terms of being able to make certain statements about environmental contaminants versus other things that could

cause comorbidity or whatever? I mean, you know, this is -- I'm already leaping from now we can do this to how are we going to talk about it. So I'm just wondering if you've had some thought about these things?

DR. GERONA: It's a very good question. Believe me, I've been tempted so many times. I have a sample of a patient with me, right. I have a database that has 7,000 pharmaceuticals. I have reference standards for 350 of them, so I can confirm, okay, I wonder if she is an Ecstasy user, or I wonder if she's abusing cocaine too.

Of course, a lot of these studies are limited by your IRB, what's in your IRB. You know, for example, in this particular study, we can -- we are poised to actually analyze for pharmaceuticals. Technically, there's nothing preventing us from doing that. But will we do that? No.

Because the IRB does not explicitly say that we can screen them for pharmaceuticals as well. And, in fact, you would have a hard time recruiting women if you tell them that, you know what, I'm going to screen if you're an MDMA user too or a potential MDMA user too. So it's the IRB that should be very explicit on what kinds of toxins, what databases you have.

Having said that though, there's always an opportunity, and I don't know what the legal repercussions or what the ethics behind this, to add some changes to

your IRB, right.

For example -- and I'll give you a clear case. We are -- we have done several studies on particular toxins. And we've also been interested on pharmacogenetics, for example. Is the pharmacogenetic makeup of a particular patient or a particular subject in the cohort also contributes to the metabolite that we're measuring? Which sometimes would actually determine whether a particular substance -- why a particular substance will be toxic to one but not the other. You can certainly add that.

We also -- I'm not sure if you have heard of this DMET Chip. It's a drug metabolite enzymes transporters. And it's a chip that can do almost similar to this. It has about 2,000 to 3,000 polymorphisms. It can actually screen for polymorphisms, which I think is a wonderful thing also. I mean, I think that should be the next stage in all of what we're doing to see how pharmacogenomics also play in the toxicology behind all these chemicals that we're screening for.

Again, so as far as your IRB is explicit about what you can do, then you're limited with that. That's the only screening that you can do.

But as I've said, because you can do retrospective analysis on this. If some day you'll get

that approval to screen for another set of toxins, then you can just look back to your data. The data is there, right? You just have to have, one, the database to screen for it, and, second, the IRB approval that you can actually screen for the specific types of compounds that you want to screen for.

PANEL MEMBER QUINT: Thank you.

CHAIRPERSON LUDERER: Maybe we'll take some comments from the public if we have any right now, and then we could have some additional discussion. So thank you very much again. And we'll probably have more questions for you.

Do we have any?

MS DUNN: We have just one.

CHAIRPERSON LUDERER: Okay. This is from Davis Baltz of Commonweal.

MR. BALTZ: Davis Baltz, Commonweal. This is a very down-to-earth mundane question. Thank you, Dr. Gerona. But I wonder if you can tell us the relative costs approximately of these different platforms?

DR. GERONA: It's definitely not parts per million. It's millions -- no, I'm kidding.

So you're aware that each of these companies would probably have different quotations depending on whether you're an academic institution or a private firm.

For -- I'll give you some ballpark estimates. For example, the TOF-MS from Agilent, the 6230 that's depicted there, I think, is one of the cheaper of these instruments. At the ballpark it will probably cost you about $300,000.

The 5600, see -- and I don't want to be quoted for this, because I might get in trouble with the different companies. It will really depend on what applications also you want to perform, because, you know, you might need another type of ion source or you might need a particular software, so the software are actually sold separately as always, right?

So you can buy the hardware, but the software to operate it and the software to dig data for is also being sold separately. To me it's counterintuitive. Like why would you buy me -- sell me the hardware without the software to operate the instrument.

So to make -- so I think probably between half a million, about 700,000 depending on what applications you want. The OrbiTrap is much more extensive. And, you know, I don't have a ballpark estimate with me for what the OrbiTrap would cost. And that 500,00 to 600,000 would probably include also the liquid chromatography portion of the instrument, because you would want to run this with an LC, but that's probably just --

MS. HOOVER: Speak into the mic, please.

DR. GERONA: Sorry. Probably about 80 to 120,000, depending on what capability you have. So that's all included in that 500 to 600,000 probably that I was quoting. But then again, you know, it will depend on your arrangement with the company, the capability that you want, the instrument to have and the applications you want to use it for.

CHAIRPERSON LUDERER: Okay. Thank you. We have time for more Panel discussion.

Dr. Solomon.

PANEL MEMBER SOLOMON: I'm curious how many other folks are out there that you're aware of who are using this kind of methodology to look at biological samples. Are there other groups at academic centers or other places that are sort of proceeding in parallel and working on this?

DR. GERONA: Okay. I can answer for the clinical toxicology part. I am not aware of any other group in environmental toxicology that are doing non-targeted analysis. But the TOF can also be used for targeted analysis. And there is ARUP. ARUP is a reference laboratory. They actually have developed a method for screening pain management drugs in serum. It's already being offered. It's on line since -- I assume. I

can't -- gosh, I can't remember. I think March or even earlier than that.

So they've used the TOF to develop a panel for drug screening. There are other laboratories that are actually using it for developing methods for drug analysis.

I know that the Millennium Laboratories in the south, which is another reference laboratory, has the instrument and has developed a method for it. I don't know whether their method is on line or not.

NMS has just purchased the Agilent TOF also, I think March. To give you an idea on the interest of this kind of machine, in our field there is an association called mass spec for academic and clinical laboratorians.

In 2010, when I attended a conference, there's hardly any poster on the TOF or the OrbiTrap. 2011, last February, there's probably about 25 percent of the posters that are devoted to this type of technology. Whether they are doing non-targeted analysis of environmental toxins or not, I'm not certainly aware.

You know, environmental toxins it's not just the application that you can do here. A lot of people who have this machine actually use it for metabolomics. So if you have researches where you would want -- for drug discovery as well. If you researches where you want to

follow a particular compound in say a cell, right, and look at what particular metabolites are being produced or more importantly say you have a cell that is sick and a healthy cell, you can actually compare all the masses that are in the healthy cell and the sick cell, try to compare them and look for are there unique masses that are developing in sick cell that are not found in the normal cell or are there missing masses in the sick cell that are in the normal cell.

I think this technology would transform the kinds of researches that we can do. And we're just at the beginning stages of it. And we're very glad that we can actually apply it to environmental toxins in biological matrices.

CHAIRPERSON LUDERER: Dr. Bradman, do you have a question?

PANEL MEMBER BRADMAN: I had a question and then a comment.

The question was you mentioned at one point though that depending on the extraction method, that might determine what you find. So it seems like there still is an inherent limitation there. You're not necessarily measuring everything that's there, but we're measuring what you can extract. And we may not know what's getting extracted by your solvent or method.

DR. GERONA: And that's why the approach is to use multiple methods of extraction, so you're covering -- and complementary ones, so that you're actually covering what the other may lack.

PANEL MEMBER BRADMAN: Right. Just we should kind of keep that in mind.

DR. GERONA: Oh, yeah. There are certainly limitations to this technology. Also, one limitation, for example, is that if you just have -- so there are machines that are TOF alone, where it's devoted to intact ions. There are also machines that are QTOF where you have intact and other ions. If you have the TOF alone, there is a co-eluent, meaning a molecule that has the same molecular weight as your molecule of interest, that would interfere in the ionization of your environmental toxin, you might miss your environmental toxin. So that's also a limitation.

So if I were to buy a TOF, I would buy a QTOF, because that gives you more power in terms of actually interrogating further like, you know, can -- based on the daughter ions, can I say and go back and say actually I have this compound. It's just -- you know, there's just a co-eluent that's isobaric with the compound that I'm interested in.

PANEL MEMBER BRADMAN: And the comment, maybe

this is more discussion related to Dr. Quint's comments. I think it does raise fascinating ethical issues. But I think a priori, if you're consent forms, you know, address measurement of environmental toxicants and you defined a pre-existing library that may exclude, for example, pharmaceuticals or illegal drugs, you know, then those are the compounds you focus on, and those are the compounds you focus on quantifying.

And I think that there is an approach, because I know this comes up in a lot of, you know, biomonitoring health studies. And certainly it's been a challenge to us when it's come up as an issue. And that's essentially the way we've addressed it, you know, put constraints on the consent form and then, you know, you're obligated to follow those.

However, I think from a research point of view, there are opportunities to collect or obtain anonymous samples. And that might be an opportunity to expand the library and potentially identify other compounds and environmental toxicants in particular, that could then be focused on in a -- you know, in a biomonitoring survey that was specific to a population and involve returning results and that sort of thing.

CHAIRPERSON LUDERER: Dr. Quint.

PANEL MEMBER QUINT: Julia Quint. Yeah, one of

the reasons I asked that is because in occupational biomonitoring studies one of the things that a lot of workers are sometimes, you know, concerned about, because of the drug testing in workplaces and things like that. You know, so testing for other -- things other than what you said you're going to test for is sometimes an issue, so I think -- the other question is you mentioned that this is a really good tool to be -- to complement targeted biomonitoring.

DR. GERONA: Yes.

PANEL MEMBER QUINT: So in our situation, where you're sample size is, you know, an issue, do you know now whether or not one sample collection would accommodate targeted versus the TOF, whether -- you know, you're perceived -- the non-targeted or would we -- are we still at the phase of doing this separately from targeted analytes or targeted biomonitoring?

DR. GERONA: So if I understand the question, correctly, would a single sampling of a subject be enough --

PANEL MEMBER QUINT: Right.

DR. GERONA: -- for a non-targeted analysis --

PANEL MEMBER QUINT: Exactly

DR. GERONA: -- so say that, okay, this compound might be present?

PANEL MEMBER QUINT: Well --

DR. GERONA: Is that the question or --

PANEL MEMBER QUINT: Yeah. I guess I'm trying to have everything. So, you know, if you have the sampling, the sample size and getting the sample is one of the big issues here, how much sample and what can you do with one sample? So we're now aliquoting samples, so we can do many different analytes and that sort of thing.

So if we wanted to answer both questions, you know, because in this program we have to do targeted, you know, because that's what the legislation says.

DR. GERONA: I guess now I understand your question better. You're actually asking me about the sensitivity of the instrument whether, you know --

PANEL MEMBER QUINT: Yes.

DR. GERONA: -- would I require 500 microliters of blood --

PANEL MEMBER QUINT: Right.

DR. GERONA: -- or 3 mls of blood? And so if I require 3 mls of blood here, then I won't have enough sample for a targeted analysis.

Okay. So the answer to that question is it depends on which platform you have, right?

So right now, I think as far as sensitivity is concerned -- I should not just quote an incident. There's

an instrument that should show how you -- to probably a 1 ml sample would be enough for three different sample extraction methods.

Having said that though, different families of compounds may ionize differently and may have different levels of ionization. In practice, what we are using right now is about 750 microliters for extraction. But the instrument that we have is not sensitive enough so far. So we are upgrading on another instrument that we're expecting to bring it down to at least 500 microliters. So if we have three sampling methods, that's about 1.5 ml.

And so if you're concerned about is there anything that you can use for targeted analysis, the answer also to that is that whatever is left -- because the injection volumes, although you need 500 microliters of the sample, you need that for concentration. The injection volume for this particular analysis is between 2.5 to 5 microliters. 2.5 actually is a lot of already.

So then you would have enough sample that you've used for non-targeted analysis. If you developed a method that would have the same solvent system as your non-targeted to your targeted, you can just carry over that sample and then use that for your targeted approach. So that shouldn't be a problem.

PANEL MEMBER BRADMAN: Can you retain the

extract?

DR. GERONA: Yeah, of course.

PANEL MEMBER BRADMAN: You just simply store the extract?

DR. GERONA: Yeah. Put it in a minus 80 freezer, and -- so we still have to do stability studies of course. But from experience, we're doing -- my experience so far is on drug analysis. And again, there will be variability and stability. So it's really very difficult to give you a general answer that will apply to all chemicals. Say, for example, for the drug analysis that I'm doing, I have chemicals that are stable for six months or even more in the minus 80, and there are chemicals that are stable only for a week.

And, I guess, you know, you can -- I guess -- so the limitation here is what's the time difference between your non-targeted and your targeted, right? And we haven't crossed that bridge yet and we're very early in the stages of this study.

So our approach to that is to use 20 retrospective samples, use those samples again, and add to that 30 prospective samples, so that we will have 50 samples in the end for the targeted analysis and compare our data, I guess.

CHAIRPERSON LUDERER: Any other questions from

Panel members?

I do have just one question about your -- when you were talking about the library of 700 compounds, is that parent compounds or does that also include metabolites?

DR. GERONA: Yeah. So far, those are mostly parent compounds right now.

CHAIRPERSON LUDERER: And in order to identify metabolites though, you also need to have the metabolites in the library.

DR. GERONA: So I tell you what, so there are also software -- so, for example, AB SCIEX and WATERS, they have software -- say, for example, you put in a parent compound, they have a software that has an algorithm that will predict all phase 1 and phase 2 metabolites of that particular compound and give you the chemical formula.

So then you can actually look for those formulas in your samples, because aside from the database, what you can also do with this technology is to do individual searches of a chemical formula. In fact, sometimes, when I have an unknown, and it's not in my database, I will do some Google or Wikipedia search, because I wonder if this is this particular drug? And then just ask, okay, is this chemical formula present in my sample or not?

And it should be able to provide you an answer of whether it's a possibility or not. So there are a lot of -- you know, the first time I learned about this instrument, it's love at first sight.

(Laughter.)

CHAIRPERSON LUDERER: Dr. Solomon.

PANEL MEMBER SOLOMON: Yeah. My question is for the Biomonitoring Program folks, because I remember we had had a discussion at one point about concerns from CDC that using these kinds of approaches could constitute research which would not be within the scope of our CDC grant.

And so I'd just love to have a little bit of discussion and creative thinking about ways that perhaps we could use this type of approach in the Biomonitoring Program.

DR. DAS: Rupa Das, Department of Public Health.

Yes, that's correct. The CDC cooperative agreement is not -- our guidance is that we are not to use those funds for research. And currently, the latest guidance from the project officer is that a TOF would be probably considered research. And so we're looking at ways to possibly get around that. But currently the guidance is the TOF would probably be considered a machine for research.

However, we could look at other funding sources

to fund that instrument. And we -- you know, I'm not sure that the issue with CDC has been completely resolved regarding our ability to use those funds to buy a TOF. But currently, it's not a given that we would be able to use those funds to support this instrument.

CHAIRPERSON LUDERER: Dr. She, do you have a comment.

DR. SHE: Yes. I mentioned we also evaluated our last purchase. One instrument that we evaluated is the OrbiTrap, because the high resolution of the OrbiTrap. Also, because the Program, we may be able to bring the price down into an area we can afford.

So we evaluated the OrbiTrap. We also gets quotation for AB SCIEX. We sent certain targeted analytes. For example, we send the OrbiTrap, which are produced by some official, we send them all of the environmental phenol samples -- oh, sorry OP pesticides for target analysis.

So at least we are -- if they can't do the target analysis, we are aware the linear range is lateral. But the three like here can reach tens -- 2,000 to 12,000 in the linear range. So so far we get the results back for the OP pesticides.

And also we send the perchlorate chemicals to them, which we already know the result. And we are

evaluating this result.

And for the Agilent TOF under AB SCIEX we send them samples too. But we tried to talk with CDC to see if they can agree if this machine can do certain target analysis with extra feature, can do the low target analysis.

Also, I think Dr. Gerona mentioned beyond the unknown compound analysis, the obvious group of machines can do confirmation. So when we do our target analysis, we depend on each transition, which is like 2 ions, parent ion plus daughter ion. Somehow this information is not enough.

So to say is this a chemical we are looking for as a target, even plus as a reference? So we do need it even for target analysis alone. I think laboratory need something it can conform, because you have a high resolution high acute mass -- now within this high acute mass, you know that only a few congeners or chemicals can match it, so you know your target analysis is more accurate. So we may try to send this one to CDC to see if we can get this through.

Thank you.

DR. GERONA: That's a very good point. I'm not saying this because I'm a laboratorian and I'm supporting the other laboratorian. We are actually developing

methods using targeted analysis for using the TOF.

And I can tell you now, when I'm done with the mini validation of a seizure panel the we can do semi-quantitative analysis using the TOF. So I don't know what level of accuracy folks from this group require, but you can certainly use this machine at least now for semi-quantitative. We are still assessing how this machine will compare as far as quantitative analysis is concerned with LC-MS/MS.

And I think for that, we are waiting on the 5600 compare it with the 5500. And if we're thinking that they're comparable, then we would certainly use it also for quantitative analysis.

And, I guess, if you can phrase it that way, that you are using this for confirmation in your analysis, then I don't know maybe CDC would be convinced that it may not just be a research tool.

CHAIRPERSON LUDERER: Dr. Solomon.

PANEL MEMBER SOLOMON: I'd like to propose a formal recommendation from this Panel. That the Biomonitoring Program explore ways to use these TOF or OrbiTrap technologies for priority setting and for confirmatory analyses. And that in the near term that these could -- you know, this could be done through partnerships with other outside institutions, and

ultimately through the purchase of, you know, appropriate laboratory instrumentation.

I think that it might be helpful, you know, if the Panel supports this, for the Program to, you know, understand that we view it really as -- you know, both as a priority setting tool for us to use really, as we designate chemicals and prioritize chemicals within the program and also as an important laboratory tool and not as a research tool.

CHAIRPERSON LUDERER: Dr. Das.

DR. DAS: I'd like to respond to one of the -- well, thank you for that. We'll take that guidance and use it for the Program.

I just wanted to let you know that CDC's priority is to have high throughput instruments. And so, again, we can certainly look if CDC isn't -- CDC's waiting to get the results of our exploration to see if they would approve this purchase. If not, there certainly is the option to look at other resources beyond CDC. But their primary concern is to develop state capacity and capability for biomonitoring, and so they really wanted to push for high throughput.

CHAIRPERSON LUDERER: I know we need to move on soon, but do we have other comments from the Panel?

PANEL MEMBER McKONE: Well, I mean, since this is

a recommendation from the Panel, I mean, I agree with it, I think we should at least have some verbal discussion of it.

So if the CDC -- so in further response to Dr. Solomon's point. If there are others -- if CDC is pushing this direction, does that mean we need separate capacity in California or can we take advantage of it or are there -- they're only seeing it as being done here, right? They're saying they're going to give money for equipment in California to do the rapid screening?

DR. DAS: Maybe I should clarify my comment. The purpose of the CDC biomonitoring cooperative agreement is to build capacity at the state to do biomonitoring. By that, they mean to have high throughput capacity.

PANEL MEMBER McKONE: Right. And are they building -- I'm just -- are they building a similar capacity at sort of a national level?

DR. DAS: They did NHANES. NHANES is performed at the CDC. In addition, they do sample analysis for other states. Part of the purpose of the CDC biomonitoring grant was to push that ability out to the states, so that they wouldn't have to do as much biomonitoring for others.

PANEL MEMBER McKONE: Right. But we're also talking about different technologies. So their

technologies are all high throughput?

DR. DAS: Yes.

PANEL MEMBER McKONE: So we're just trying to get that.

Now, the other point though about, I think, that's important is that this is an adjunct to -- you know, we spent the first year developing a screening process, which was really not analysis based. It was really based on going through the CDC's records, going through uses of chemicals, going through modeling. I think it is important to point and emphasize that this is another way of coming at that, an adjunct to that whole process -- an important adjunct to that process, to do some rapid screening to see what we find as opposed to searching through lists of chemicals to flag the ones that we think are --

CHAIRPERSON LUDERER: So just to clarify, the CDC is talking about high throughput targeted, right, as opposed to unknown?

DR. DAS: Yes.

CHAIRPERSON LUDERER: And I actually kind of wanted to agree with what's been said so far, and also to say that this morning, I think there was -- the example that Dr. Petreas was talking about, trying to decide which of the additional brominated flame retardants, you know,

organic flame retardants assays should be developed for, and the difficulty of developing these assays. A method like this could be used for prioritizing, you know, which ones are actually detected in -- you know, in biospecimens, and then developing the targeted assay for those, rather than, as may already happened with some of the targeted assays that she was talking about this morning, where they may not end up being able to detect those compounds and biospecimens.

Any other comments from Panel members?

PANEL MEMBER QUINT: This is Julia Quint. I just want to add too also, we are constantly challenged with use and potential exposure questions, you know, because we don't have any sources in the country, let alone the state, of finding out what chemicals are used and where they're used. And so this would help get around that. And I don't think we're close to getting that information.

We've had bills in the Legislature and other means of trying to -- you know, because it's definitely the essential piece in priority setting. You want to be able to go after things that are relevant to the California population. And I don't think we can get as -- anywhere a handle on that, you know, to the extent that we can get it with this technology.

So in talking about this, I think that issue

should come up as well, you know, how difficult it is. Every program I've worked in, in this issue of chemical exposures, the question is, is it used in California? If so, where, and how much and who's exposed, and you can never get at that.

So this would be one of the ways -- a great way of being able to do that, which I don't consider research. I consider essential to the task.

CHAIRPERSON LUDERER: So we did have a suggestion for a formal recommendation from the Panel. Would you like us to -- should we have a formal vote on this?

MS. HOOVER: Yeah.

CHAIRPERSON LUDERER: Do we have a second from a Panel member for a vote?

PANEL MEMBER McKONE: I think I seconded it.

CHAIRPERSON LUDERER: Dr. Bradman, would you like to vote -- start voting and we'll go down.

PANEL MEMBER BRADMAN: Yes. I just have a question, is the wording of the recommendation clearly enough for the Program?

MS. HOOVER: Yeah. It's clear enough to me. If you want to restate it, sure.

PANEL MEMBER SOLOMON: Actually, I'd like to add one more thing to the wording based on what Dr. Luderer said, and something in Dr. Gerona's presentation, which is

that this is an important technique clearly for any chemical for which there's no reference standard. And we have already prioritized many of the brominated flame retardants. And we heard this morning from Dr. Petreas that there are no reference standards for many of our priority chemicals.

And so there appears to be no other way to feasibly monitor for those chemicals, absent the use of a QTOF type method or OrbiTrap type method. So I think that's perhaps something we should add.

CHAIRPERSON LUDERER: Okay. So is that clearly stated, so do we want to have it summarized again?

MS. HOOVER: Sure. I mean, if you want to just restate it. I mean, what I wrote down was that Biomonitoring California should explore ways to use, I guess with TOF, QTOF, OrbiTrap and similar technology for priority settings and confirmatory analyses. And with the added note that use of these technologies is the only way to look at some of the chemicals on our priority list because there are no reference standards.

CHAIRPERSON LUDERER: Dr. McKone.

PANEL MEMBER McKONE: I'll second that. It's revised, I think it has to be re-seconded.

CHAIRPERSON LUDERER: All right. I think we're ready to vote.

So Dr. Bradman?

PANEL MEMBER BRADMAN: Yes.

PANEL MEMBER SOLOMON: Gina Solomon, yes.

PANEL MEMBER McKONE: Tom McKone, yes.

CHAIRPERSON LUDERER: Ulrike Luderer, yes.

PANEL MEMBER QUINT: Julia Quint, yes.

PANEL MEMBER KAVANAUGH-LYNCH: Mel Kavanaugh-Lynch, yes. And I would add in terms of the expense, having an evidence-based priority setting methodology would save actually the State large amounts of money.

CHAIRPERSON LUDERER: All right.

That was -- I'm sure we could go on discussing that for quite some time, but we do have to move on to the next topic. We do have a break scheduled. I wonder should we make it a little shorter? Should we do a 15-minute break?

MS. HOOVER: Let's still do 15 minutes.

CHAIRPERSON LUDERER: So it's 5 to 3 by this clock. Shall we say 10 after 3 then we'll reconvene.

(Thereupon a recess was taken.)

CHAIRPERSON LUDERER: It looks like people have come back in. And I'd like to welcome everyone back from the break. And I wanted to reintroduce Sara Hoover, Chief of the Safer Alternatives Assessment and Biomonitoring

Section at OEHHA.

Sara.

(Thereupon an overhead presentation was Presented as follows.)

MS. HOOVER: So I'm just going to introduce the Panel discussion. So referring you back to the March 17th workshop what we had on understanding and interpreting biomonitoring results, because the Panel attended in the audience, you didn't have a chance to actually talk about this workshop as a Panel, so that's the purpose of this item.

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MS. HOOVER: So we want to give you time to discuss it as a Panel and give us any input and recommendations about the workshop, anything you'd like to highlight about the workshop that particularly struck you.

So to help you start your discussion, what I'm going to do here is just give you a very brief overview of some of the March workshop highlights, and also a very brief outline of the direction of Biomonitoring California on these issues.

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MS. HOOVER: So just to remind you the background for the workshop. You know, we were interested in talking about these issues for a few reasons. One is we're going

to be returning individual results to participants upon request, and advising individuals on follow-up steps as needed. And we're also going to be using biomonitoring results to help support the State in evaluating public health efforts to reduce chemical exposure. So both of these activities will require understanding and interpreting biomonitoring results.

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MS. HOOVER: The March 17th workshop included presentations by six national experts, and a number of discussions with the speakers and the audience during the workshop.

There's a website devoted to the workshop that includes all the presentations, the transcript, and a brief summary.

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MS. HOOVER: The objectives of the workshop were to discuss approaches for understanding and interpreting biomonitoring results, discuss possible methods for developing comparison levels in blood or urine, consider scientific challenges in interpreting the results, such as how to address multiple chemical exposures in sensitive subpopulations, and just generally provide input to Biomonitoring California on these issues.

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MS. HOOVER: So you probably saw in your packet and also we posted on line a brief summary. And the way that we did the summary of the workshop was really to draw on the discussion periods and highlight some of the issues of interest. Now, this is not definitely a comprehensive summary, and we'll be continuing to look at the very rich transcript and speaker's presentations.

I'm just going to go through some of the topics that we did pull some highlights out on.

The first was returning individual results, particularly giving context and uncertainty; information on chemical health effects and exposure sources for report back; developing levels of health concern; evaluating exposure sources and studying early effect markers, and aspects of biomonitoring measurements, and how biomonitoring results will inform public health and regulatory actions.

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MS. HOOVER: So now I'm going to do an even briefer summary than what we prepared in writing and just pull out a couple of things in these general areas.

So in terms of individual results return, one of the things that was discussed was how important it was to convey the uncertainties in the interpretation of biomonitoring results when returning individual results,

and that people are able to process and understand the fact that there will be these uncertainties.

That we should provide context for individual results, such as results from the study population, NHANES, and other relevant populations.

And that most people will likely want their results, as well as more information on the chemicals being biomonitored.

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MS. HOOVER: In terms of interpreting health effects, there was a note that advice on possible health concerns can be more easily provided for well known hazards like lead and mercury. And there was a number of comments from the audience, as well as the Panel, at the previous Panel meeting, and at the workshop, that developing levels of health concern for individual risk interpretation should not be a program focus.

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MS. HOOVER: In terms of exposure sources, one interesting point of discussion was that following up on "Who's High and Why?", can provide very useful information on exposure and maybe identify some unique exposure sources.

Another approach would be to remove known sources and monitoring the effect on biomonitoring results. And

that that process can reveal some key sources and possible ways to reduce exposures.

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MS. HOOVER: There was a lot of discussion of analytical issues. Here's just a couple of things, and aspects of the measurements themselves.

So it's really important to understand and take into account how analytical issues like level of detection can affect the interpretation of the results that we get.

And that we might want to consider a study design that includes multiple measurements in each person to better estimate variability, so instead of just increasing your N to actually have multiple measurements in individuals.

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MS. HOOVER: In terms of public health and regulatory action, there was a lot of discussion about why is Biomonitoring California important, and why was it established? And this can influence how we look at the results.

So some of the things noted were that the Program was established to help investigate possibly higher exposures in some communities, to set priorities for which chemical exposures warrant action, and to generate data on emerging chemicals, so that it's important for the Program

to really think strategically about what questions we can answer and how those questions relate to regulatory and public health policies.

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MS. HOOVER: So just a note, that a lot of the feedback we received at the workshop was really consistent with the direction we're heading, in both individual results returned and also these larger issues.

So just a reminder, basically very brief note on the direction, which is that the Program intends to continue to focus on generating data to understand levels of chemicals and trends in communities and the general population, and to support the evaluation of public health and regulatory programs, that those main goals of the Program remain.

We also have an obligation to our participants to use best practices to return individual results, and to do follow up where needed. And you heard some of that work we're already doing in Dr. Das' presentation. And you'll hear a lot more about that in the future.

So at this point, I just want to turn it over to Dr. Luderer and let her facilitate your discussion of the workshop.

CHAIRPERSON LUDERER: Thank you, Sara.

Do we have any comments or discussion from the

Panel members?

Dr. Quint.

PANEL MEMBER QUINT: This is Julia Quint.

I just want to compliment the Program on a very -- I thought very productive workshop. I think the choice of the speakers, they were varied. And I thought each of the presentations, while I didn't agree with everything that everybody said, I think they all had -- made very unique contributions. And, you know, the content of their presentations were very helpful.

And I think it also confirmed, I think what Sara just said, that we are headed in the right direction. It really, for me, helped to distinguish between the amount of emphasis that we should be placing on interpreting individual results and trying to come up with what does this result mean in terms of a health outcome, and the focus on, you know, public health and population, what this means for a large group of people, as opposed to the individual. Even though, we have an obligation and will return results to individuals, and will do -- you know, have appropriate information about the chemicals and how to reduce exposure and things like that, and following up on high exposures.

This really is about, you know, what we're doing in terms of protecting California as a population from

environmental contaminants where we can and evaluating what we're doing, and what we have done.

So I think that the workshop participants really confirmed that, you know, and how difficult it is, for instance, to -- if you're interpreting results, in terms of using old risk assessments, and -- you know, to make statements about whether or not results are high or low, in terms of interpreting them for individuals.

This is a good -- you can do this when you want to look at setting priorities and maybe as a research follow up, but not for giving relevant information to an individual about, "Oh, you're very low and no reason for concern", or, "This is very high".

So, for me, I thought it was really helpful. I understood the biomonitoring equivalents much better, and how they -- you know, and the caution, in terms of their use as -- you know, in terms of telling people about potential health outcomes.

So, for me, it was very -- it was a very good experience.

CHAIRPERSON LUDERER: Any other comments from Panel members, discussion?

Dr. Bradman.

PANEL MEMBER BRADMAN: I just want to follow up on what Dr. Quint said. And, you know, I certainly came

out of the workshop impressed by the breadth and depth of what was presented, and also still agree with this summary that, Sara, you included here, that developing levels of health concern for individual risk interpretation should not be a Program focus.

And I remember that kind of lit up some discussion, actually in this room, last year. And maybe we want to follow up on that and really assess whether there's consensus on that on the Panel.

Just personally, I have a concern that if we get into the business of, you know, risk assessment -- that if the Program gets into the business of risk assessment, that it might become more difficult to actually do the biomonitoring. And that if there's any risk assessment going on around these measurements, that they should be in a different context and not linked directly to the Program, because of the, you know, debate and process and input.

One thing where I see a certain tension or conflict though, and maybe we need discussion here, is that if there is an interest in providing some interpretation to individuals, how do you provide that interpretation without that becoming a precedent for some other decision that might be unrelated to the Biomonitoring Program?

So I guess I'm putting that out there as something maybe we should consider.

CHAIRPERSON LUDERER: Dr. Solomon.

PANEL MEMBER SOLOMON: Yeah. I agree. It was an excellent workshop. Very good summary. And that I still feel -- agree with Dr. Bradman and still feel quite strongly that we shouldn't be in the business of trying to, you know, get too far down the road of, you know, quantifying or, you know, providing health-related benchmarks as part of this program. And so -- and for the same reasons that he stated, which, you know, largely have to do with resources and with sort of pulling us off track, but also with some more substantive issues, including the fact that, you know, we have intentionally chosen to biomonitor for chemicals that are poorly understood. And so there wouldn't be sufficient information on which to base enough of a risk assessment that we could come up with a biomonitoring equivalent or any such number. And so I think that we do need to keep our public health focus.

With regard -- well, I'm not quite sure how to answer the question that you raised, so I'll sort of see if other Panel members have other comments on that.

CHAIRPERSON LUDERER: Dr. Quint.

PANEL MEMBER QUINT: I'm not sure I -- this is

Julia Quint. I'm not sure I can answer the question, but I have had experience in -- when I was with the Department of Public Health of answering questions from people that people posed about chemical exposures, albeit in an occupational situation.

But having done that for, you know, 15 years or so, I think there -- for me, it's the -- you separate toxicity from health outcomes. I mean, the reason we have chosen certain chemicals is because of their potential toxicity of -- because of their toxicity and potential to impact health.

So often -- I mean, I make a big distinction between those two things. I mean, the chemical is toxic, is there exposure? And often you can't answer how that particular exposure, if there is exposure to that toxic chemical, how that will impact one's health, because we don't have those studies.

I mean, we have some epidemiological studies, but even those you can't say to a person, to an individual, whether or not they will be affected. So I think you have to give them the information you have.

This is, you know, why we measured this chemical and you'd -- and we will have chemical-specific information about the toxicity of the chemical. And to the extent that we can, I think the emphasis should be on

potential exposure to that chemical, how is the exposure -- how does exposure to that chemical occur, and to help emphasize, you know, lowering exposures where that is possible.

So I think that's fine. I mean, I don't think you can go beyond what you actually know. And I don't think we should go beyond what we actually know. And most people are satisfied with that.

I mean, that is not -- it's been my experience, anyway, that people don't become really frustrated and irate because you can't say, "Oh, yes, you will get cancer in 10 years", or whatever, or "This will be the outcome".

I think it's very appropriate to stay within the bounds of the toxicity concern and to help ferret out whether or not the person -- and if it's in your body, you obviously have exposure of some kind, depending on the level.

But just saying where -- how that exposure might occur and what you might do, as some of the speakers said, to reduce that exposure, I think, is going -- in most cases, is going to be okay and is where we should be.

CHAIRPERSON LUDERER: Dr. Kavanaugh-Lynch.

PANEL MEMBER KAVANAUGH-LYNCH: So I'm not sure I understand the precedent-setting question. Can you state that in a --

PANEL MEMBER BRADMAN: If results were returned to an individual and there was an interpretation like this is safe or unsafe or of concern or not concern, then the number, the cutoff, the threshold that was used to make that conclusion could then become de facto a reference number or a benchmark or a point of departure in a risk assessment context outside of the Program, and without having received, you know, sufficient scrutiny and review, that it might deserve if it was being used in that context, or outside that context, I guess I should say.

PANEL MEMBER KAVANAUGH-LYNCH: Okay. Well, I think I agree with everyone else who's spoken thus far, is that stating the risk associated with levels is not in the purview of this Program and shouldn't be done, except to reference known reference levels from others.

CHAIRPERSON LUDERER: I mean I think overall there seems to be -- I think there's a consensus on the Panel that the summary, you know, that you provided, I think, that -- and the direction that the Program is going in is one that we're all in agreement with. And certainly I think everyone on the Panel has commented that setting reference level or health limits should not be a main focus of the Program, and really it's not within the legislative mandate of the Program, I would say.

Do we have other comments?

OEHHA ACTING DIRECTOR ALEXEEFF: Sorry, I have a comment.

Well my comment is that with regards to the reference levels and that sort of thing. Since it's a -- basically a State program, and that we're focusing on smaller samples right now, I think the intention is providing -- advising information to an individual is much different than trying to reduce a population-wide exposure. And I think we're thinking about population-wide exposures, and trying to reduce them.

So that should be, I think, more the focus. And if we were able -- you know, like, for example, even the lead studies, we were able to find the neurological effect, because you have a large population with a lot of information, that's going to be very, very rare, and instead you'd be dealing with very small bits of information and trying to come up with a level that probably would not be overall good for the whole society to be at that level.

CHAIRPERSON LUDERER: Dr. Quint.

PANEL MEMBER QUINT: This is Julia Quint. I'm not sure we satisfied Asa's -- Dr. Bradman's -- that we answered to your satisfaction. So why don't you give us some feedback on that.

PANEL MEMBER BRADMAN: No, I think you did. I

think Dr. Solomon maybe perhaps reinforced what I said. But again, my point is that if there was a health interpretation that was provided when individual results were returned back, could that then -- I would be concerned if that then could become a precedent for other benchmarks or point of departures or other risk assessment guidelines in other programs, like in other pieces of OEHHA, for example, where they set reference doses or an NSRL or an MADL. And then that could become a -- it could be -- it could become a fight within the biomonitoring program to set a standard. Am I being clear here?

In other words, I'd be concerned that somebody could come to another program and say, "Hey, you said this was safe to these individuals", therefore there's a precedent here.

And in another program, you may or may not come up with that level with a more thorough review.

And number two, then -- if those kinds of decisions were being made within the Biomonitoring Program, I'm concerned that it could politicize or complicate the process of returning results, because then there would be a lot of interest groups that would want to weigh in on how that was established.

So I want to just be sure that my recommendation is that the possibility for that be separated from the

Biomonitoring Program, the possibility for politicization or the kind of scrutiny and debate that actually goes in to setting an accepted benchmark dose or threshold.

Is that clear?

PANEL MEMBER QUINT: Right.

CHAIRPERSON LUDERER: Dr. Quint.

PANEL MEMBER QUINT: This is Julia Quint. It just prompted another question for me. So are we, in returning results, did -- because I don't remember the exact presentation format that Dr. Morello-Frosch and Holly presented, but are we going to have thresholds of safe and not safe? I mean, how are we -- is there -- will there be an attempt to compare levels to reference doses and that sort of thing?

I didn't think we were exactly heading in that direction, but I may be not remembering correctly.

DR. DAS: Rupa Das, California Department of Public Health.

So to answer your question, Dr. Quint, the template that Dr. Morello-Frosch provided is a guide, and we will probably embellish it. So that's not the final word.

But the plan right now is to provide the levels of the individual participant compared to the levels found in that particular study population, and to compare it

with the NHANES number or another population -- relevant population. But those are the populations we're focusing on right now.

And if there were values available, such as this morning I presented the notification level for mercury, that is established by CDC, we would consider putting that in. But at this point, our focus is not on developing health-based levels, beyond what's already been established by other agencies.

PANEL MEMBER BRADMAN: Yeah. And I think that's what we agree with. Yeah. But my concern is that just that we kind of state that clearly. And this came up, you know, last year.

And then also that, for example, the presentation on the use of biomonitoring equivalents, I think that kind of analysis can be done at the population level, but not at the individual level.

PANEL MEMBER QUINT: Right. This is Julia Quint again. I think that's a valid point, because, as I understand it, from the presentation, these -- you know, there are contracts with other programs like Health Canada and maybe some European countries too, have on the website, you know, an analysis of biomonitoring results and to compare them with reference doses. So far, the biomonitoring results are well below any reference dose.

So most of their data seems to indicate that, you know, everybody is at a safe level, you know.

And so I think there might be an opportunity for people to look at whatever is put on these websites and to maybe make those comparisons. But I think we should make it clear that that is not the direction; that, you know, there are issues with those. And a lot of these were brought out by Dr. Hattis and other people.

So I think that maybe we have to have some overt statement to that effect, that this is not our interpretation of how the data should be used. Maybe we should be, you know, not just have the workshop and have this as, you know, we're heading in the right direction, but maybe say something more affirmatively about the fact that, you know, we don't necessarily agree on an individual level that you can use reference doses and -- you know, you make -- that biomonitoring equivalents is not our interpretation of how you decide what's safe and not safe.

Because I think, as far as I could see from the presentation, that these -- the information that would appear on websites is geared, not only towards individuals, but to physicians as well. So I think, you know, your concern, Dr. Bradman, that you brought up, I think is a legitimate one. So how can we separate

ourselves from that, I think is an issue.

CHAIRPERSON LUDERER: Sara.

MS. HOOVER: Sara Hoover, OEHHA.

I just wanted to follow up with a couple comments on it.

First, Lesa Aylward, who, you know, works on biomonitoring equivalents made it very clear, and I have it in the summary, that they're not intended for individual interpretation. They never have been, and the only thing that these are doing is they're translating existing risk assessments, with all of the attendant problems, into levels that are consistent in blood or urine.

So the website that they were talking about really was their realization that the BEs are not useful for individual risk interpretation, and that they were going to try to gather, you know, any other kinds of information that might be useful for physicians. So they're -- in fact, they're having a workshop maybe this week to talk about that

So, yeah, I don't know that you need to make an overt statement. I think we're very clear about what would be appropriate -- you know, an appropriate use of the kinds of information, like Dr. Das referred to the mercury level. There's also an existing level of health

concern for lead. You know, there's certain things. So I see it more, and the way that we've approached it more, is looking at what existing guidance is out there and how -- you know, how does that need to come into the Program, not we're going to start trying to create new things for this specific purpose.

But I did also want to mention that, you know, for example, and I think Dr. Das mentioned this as well, that -- and I was trying to allude to this. I didn't go into a lot of detail, but we also might do a publication -- you know, we might do an analysis and look at these kinds of things and look at the limitations, you know, and do our own kinds of analyses.

So I don't think we want to say like a complete restriction on what the program is going to do, but I think we're very clear on the guidance you've given us and the guidance we got from the workshop, and also how the program interacts with other programs in OEHHA and other programs in the State. I feel like we're pretty well grounded in how we're viewing it.

I don't know Lauren or George want to add anything.

DR. ZEISE: No. And it is pretty clear that we did hear some major limitations in some of the translation of reference levels into biomonitoring levels. So I think

in the back of our minds, there's an extensive analysis that would have to take place. And again, you've given us pretty clear direction that this shouldn't be the focus of our efforts. We have so many other things to do.

CHAIRPERSON LUDERER: Any additional discussion from the Panel?

Okay. I think we can move on to our next item then. So the next item on the agenda is a discussion of by the Panel of input that we may --

MS. DUNN: Dr. Luderer, I'm not sure if we asked for public comment at all.

CHAIRPERSON LUDERER: I'm sorry. I forgot. Do we have any public comment?

Davis Baltz from Commonweal. I apologize for having skipped over that.

MR. BALTZ: Davis Baltz, Commonweal.

Thank you, Sara, for that great summary of the workshop. And I just want to reiterate what I've heard here that I attended the workshop and I think it was a pretty clear message that the Program -- the feedback to the Program was that it would be inappropriate to sort of start to take it into an assessment of risk.

There is a lot of thorny issues about communicating results, and I think the Program is grappling with them very competently. But to step beyond

the mandate from the statute itself, I think would slow the Program down and would also -- it's just not something that's mandated in the legislation.

You know, to try to assign a health -- a level of health concern to biomonitoring data, there's so many variables that would be difficult to control for, as everyone here knows, what the timing of exposure, the life stage that you're exposed, you know, even something like body weight or gender could obviously have an impact as well.

So I just -- my message is that when the Program was still a bill in the legislature, I think it was very clear that it was intended to be a program to gather scientific data and to publish it, and then let the conversation happen afterwards about how -- what steps should be taken to -- and how to use the data.

I think it would be a mistake for the Program to start to attach any kind of risk assessment discussion. And that said, as the individuals are notified of their results, the things that you've mentioned that it will be important to state the comparison with the NHANES data, which is not a health concern -- it's not a level of the health concern, that they can see how they compare with other Americans who've been biomonitored for similar chemicals.

For those groups that want to have more information, that they don't feel they get from the State, I think NGOs can play an important role, since there have been a number of community-based studies, not only in California but across the country where people have volunteered to be part of a biomonitoring study, and they have not panicked. They have taken in their results, and it's generated a lot of important discussion in those communities about what it means and what they should do next.

And to the degree that people who receive the results from the State Program are needing more information, I think Commonweal and others who have been involved with biomonitoring with communities would be happy to try to step in and help shoulder some of the conversation. It's not something that the State is going to be able -- probably to satisfy everyone to the degree that they'd like.

So just to sum up and say one more time, and I've said this before, you've heard me, let's keep the focus on having impeccable science, generating biomonitoring data that will be useful to the State. You know, let's keep an eye on special exposures that we have in California, keep an eye on trends over time, when we have the funds we'll do the statewide statistically significant sample, let's

watch how special exposures in highly exposed groups and populations are unfolding, and then compare our trends, as we do them over time, with the policies that are developed to reduce exposure and see if they're working.

So I second the comments of the Panel as well as the summary that you made, Sara, to keep the focus on generating data and publishing it, and let the conversation about risk or health concern happen at another time in another forum.

CHAIRPERSON LUDERER: Thank you very much for your thoughtful comments.

And I apologize again for having forgotten to take public comments. So we'll now move on to the next item --

MS. HOOVER: Actually, Dr. Luderer --

CHAIRPERSON LUDERER: Yes.

MS. HOOVER: -- can I just say one last thing.

I just also wanted to really acknowledge Amy Dunn, because she was a big -- played a big role in pulling that workshop summary together. So thanks a lot, Amy.

CHAIRPERSON LUDERER: Thank you.

So the next agenda item is some discussion from the Panel regarding potential input that we might want to provide for the upcoming 2012 program legislative report.

So just to give some background, Biomonitoring California is required to submit a progress report to the Legislature every two years, and this is made available to the public within 30 days of providing it to the Legislature.

And there was a link to the first report that was due on January 1st, 2010 that's on the website. And the Panel -- it was also Emailed again to the Panel.

And the next one is due on January 1st 2012. And the Program staff are currently working on that 2012 report. So the 2012 report will give updates on various aspects of the Program, including resources, guidance provided by the SGP, chemical selection, current biomonitoring projects, best practices for results communication, efforts towards biomonitoring a representative sample of Californians, progress made by program laboratories towards analyzing selected priority chemicals and public participation activities.

So in the fall of 2009, Dr. Ed Moreno, who was the Chair of the Scientific Guidance Panel at the time, submitted a letter on behalf of the Scientific Guidance Panel to the Director of the California Department of Public Health with recommendations regarding ongoing and future efforts of the Program.

And these Panel recommendations were included in

the 2010 legislative report. And at the time, just to summarize what the Panel recommended, they recommended -- or we recommended that the Program identify resources to fully fund the Program, and implement the statewide survey; continue to pursue external funding and seek ways to leverage existing resources; continue to support activities specified in the CDC cooperative agreement to increase laboratory capability and capacity; continue efforts to engage additional stakeholders; maintain and expand electronic resources, such as website, webcasting, audiocasting of Scientific Guidance Panel meetings, and increasing listserv members; and continue to meet with the SGP three times a year, continue to support the SGP in selecting, designating, and prioritizing chemicals for biomonitoring; and continue to develop results communication methods and materials.

So the purpose of the current agenda item is to discuss whether the Panel would like to prepare a letter with recommendations to the Program for the 2012 legislative report, and if so, what recommendations should be included.

And then in terms of logistics, I would use the discussion from the Panel today to prepare the letter and send it to the Program. Because of the Bagley-Keene requirements, we would not be able to send the letter

around to the Panel for review.

So with that, I'd like to maybe start a discussion on the Panel of some of the things that -- recommendations that Panel members would like to include in the letter, also get the Panel's thoughts on whether they're in favor of such a letter.

And I just thought maybe I could start out by mentioning some of the things earlier in the discussion today that the Panel had recommended that we might want to consider including in such a letter.

So Panel members had discussed earlier this morning the importance of prioritizing chemicals for methods development and analysis. And that was something I believe Dr. Solomon had mentioned, that that -- and other Panel members had agreed to have some additional discussion of that. Particularly, I think it was related to Dr. Petreas' presentation this morning.

Screening of unknowns is another recommendation that the Panel has made several times. And we heard this very exciting presentation this afternoon, and actually did make a formal recommendation about the idea of using TOF or QTOF for prioritizing chemicals for designation and selecting designating prioritize -- designated and prioritized chemicals for development as a method.

So those are some of the ideas and

recommendations that were already discussed today. And I thought we could have a Panel discussion about additional thoughts, and also about those thoughts.

Any --

CHIEF COUNSEL MONAHAN-CUMMINGS: Dr. Luderer, just a point of clarification. Since there is one more meeting of this Panel before the report is due, you could probably draft something, share it with the Committee for the next meeting, and then have a meeting -- you know, the Committee discuss it, and, you know, say if there needs to be a change or whatever. So that's a possibility, but I don't know how soon the report has to get finished.

DR. DAS: It would be a good suggestion, except that we need to have the report go up our chain of approval well before the next Panel meeting, probably about mid-September is what we're aiming for.

CHAIRPERSON LUDERER: Okay.

CHIEF COUNSEL MONAHAN-CUMMINGS: But does that letter have to be with that draft, do you think?

DR. DAS: The last report included the letter as an appendix. And we referred to the recommendations made in that letter in the report.

CHIEF COUNSEL MONAHAN-CUMMINGS: There you go.

(Laughter.)

CHAIRPERSON LUDERER: Any thoughts from the

Panel?

Dr. McKone.

PANEL MEMBER McKONE: Well, actually I want to clarify. So basically we have to craft the key ideas and the letter has to be drafted, and we just say yes or no. We can't really go through -- we can't, as individuals, say well could we revise this language? There's no opportunity then to -- I mean --

CHIEF COUNSEL MONAHAN-CUMMINGS: Well, the issue is -- can you hear me?

The issue is that under the Bagley-Keene Act, which is really not -- it's kind of awkward, but it's intended to make sure that the public is involved in deliberations and decisions made by these types of committee.

You're not supposed to do what's called a serial meeting. And one of the ways that you could do a serial meeting was to -- would be to send something around and have everybody comment on it. Even if it was up or down, that would still be a decision-making type process or deliberation.

So in order to avoid that, last time, what we did is, you know, the group gave input to Dr. Moreno, and then he just drafted something up, assuming that he had captured your ideas. And you got it about the same time

as it went to everybody else.

So it's awkward, but it's probably the best way, if we can't get another, you know, public meeting of some sort before it's really needed over at DPH.

CHAIRPERSON LUDERER: Dr. Solomon.

PANEL MEMBER SOLOMON: I feel completely comfortable, you know, having Dr. Luderer draft a letter on our behalf after our discussion today.

But I also have a question, because there are several different possible audiences for such a letter. The previous letter was addressed to the DPH -- Department of Public Health Director.

We could presumably so address the current letter or -- you know, or in addition, we could send a letter to others, such as the Governor or the Legislature directly. And so for -- and if it were the latter, then that letter could go in at the same time as the report from the Program. It wouldn't have to go into the Program and then sort of be appended. So we could think about whether it would be more -- whether we would have more or less impact, I guess, with a letter addressed to the DPH Director versus the Legislature directly or the Governor or both.

CHAIRPERSON LUDERER: Dr. Quint.

PANEL MEMBER QUINT: This is Julia Quint.

As I recall, the last time we wrote a letter, I thought there was some barrier to sending it directly to the Legislature. I thought we sent it to Dr. Horton because we were not allowed to communicate directly, but I may be in error about that.

But I had a similar question about to whom we should address the letter, and why the Department of Public Health, when it's actually three programs involved, because they're the lead agency?

DR. DAS: Um-hmm.

MS. HOOVER: Actually, the letter went to all three, I think.

DR. DAS: But it was addressed to Mark Horton.

MS. HOOVER: And just CC'd -- well, actually, I think he actually did three letters, the same letter to the three heads of the Departments. But I think, you know --

PANEL MEMBER QUINT: We could it anyway --

MS. HOOVER: Yeah, I mean, I think that they could choose to send a letter directly, right?

DR. DAS: Yeah.

CHIEF COUNSEL MONAHAN-CUMMINGS: Yeah, I don't think there's any limitation that I'm aware of that a Committee or individuals on a committee can't communicate directly with the Governor or the Legislature on issues.

And particularly, the Governor, given he, or least the prior one, appointed you all, should have an interest in his program anyway, and so you could do that.

You know, it's kind of up to you in terms of who you want to actually address it to, and who you want to CC it too. But, you know, the information does need to go to the Program. And it is managed by DPH, and then, you know, with input from DTSC and ourselves.

But, you know, it is kind of a weighing thing. But a lot of letters, such as this, end up just CCing like the Governor and a couple of legislators that might have an interest in it. And I don't see that there's any prohibition to doing that.

PANEL MEMBER QUINT: Well, if that's the case, I would strongly recommend -- I agree with sending a letter. And I think we should send it -- because this is a new administration who may not be familiar -- as familiar with this Program as the last administration, I think that it should go to the Governor and to keep members of the Legislature in addition to the Program heads, however that's done.

And, you know, in terms of the -- I'm usually very loud.

So in terms of the content of the letter, in addition, I noticed in the last report that all of the

recommendations from the SGP were listed as a separate appendix. As I recall, there was an appendix -- so from each meeting, the recommendations of the SGP were listed.

So in this letter I think a strong emphasis on outstanding job, which we've said continually -- I mean, at every meeting. I think -- and, of course, I'm sure that would be included.

But I think to emphasize not only the outstanding job, but the follow-through on the way the Program has used existing resources and obtained new resources, new collaborations to move the Program forward, in spite of the budget limitations, which has not allowed us to do the representative -- I mean, however that's said, but to really strongly emphasize the amazing progress, and that we've made -- that the Program has made, you know, to overcome the lack of resources. And some strong endorsement of -- you know, I'm not sure it's appropriate in this budget climate to restate that we need full funding for the Program. I'm torn about that.

I think that should be stated, that, you know, we don't have the funding to do the represent -- the statewide sample, but a strong recommendation to continue the funding at the level with the -- I forgot the name of the fund we're using, but to at least continue full funding at the level that we have, I think, should be a

very strong endorsement.

In other words, I'm looking at the letter as more concentrated on introducing this program and its accomplishments, and the Panel's strong, you know, recommendation of the quality of the Program, and with some emphasis on funding. And so not a lot of specific recommendations, which I think can be referred to in the other appendix, you know, because I think that will be lost, but just recommendations of, you know, endorsements, and, you know, more of the same and more funding.

CHAIRPERSON LUDERER: Dr. Bradman.

PANEL MEMBER BRADMAN: I just wanted to echo some of the things Julia said. She actually went down my list. Some of the things I think to cover would be definitely commending the Program, and specifically whether we want to get into details or not. I think building the laboratory has been an important accomplishment, in terms of personnel and space and effort.

Also, successful implementation of the CDC cooperative agreement, and the importance of that external resource to build the California program. Participating in and completing the pilot studies. Also, very successfully, and I think effectively, engaging the public on -- you know, that was a key part of the legislation. I think the Program has lived up to that.

You mentioned the funding limitations. Also, perhaps reviewing the last letter and highlighting, you know, points that are still relevant, and, you know, making sure that any issues there, you know, continue to be brought to the attention of the recipient.

CHAIRPERSON LUDERER: Dr. Quint.

PANEL MEMBER QUINT: Julia Quint.

I just want to add one more thing that we should have a strong statement about filling vacant positions and the importance of, you know, the unfilled vacancies and having full Program -- I mean, full staffing for the Program. I think that should be stated in the letter.

CHAIRPERSON LUDERER: Other recommendations, thoughts from Panel members?

I could maybe review just what I have heard from people so far. I think there was consensus to send -- to address the letter to the heads of the three Departments, but then also to CC the Governor, and we talked about some -- also, potentially legislators. We haven't talked about which legislators. That may be something we want to still discuss.

We're going to, in the letter, talk about the outstanding job that the Program has done with all the -- despite the limited resources, and identifying collaborators, identifying sources of funding, being able

to move the Program forward in multiple areas, including the lab capacity and personnel, in terms of the CDC cooperative agreement and the other pilot studies, and in their efforts to continually engage the public successfully.

We also would like to strongly endorse in the letter the idea that once the economy improves that the Scientific Guidance Panel feels that in order to really be able to accomplish the mandate of the law of having a representative sample of California residents, that full funding for the Program, at such a time when that is possible, really should be the direction in which we go. And that currently at least, that the funding level be maintained at the level that it has been funded -- at least at the level at which it has been funded in the past year.

And we also would recommend that the open positions that are currently -- the various labs and other program open positions, that they be filled, and that exemptions from the hiring freeze be obtained for those positions.

Did I capture -- Gina. Dr. Solomon.

PANEL MEMBER SOLOMON: Yeah, great job.

Just a couple tiny details. One is I think it actually might be useful to include a few bullets just

summarizing the pilot studies, so that, you know, just, you know, study on firefighters in Orange County, study on pregnant women in San Francisco, Kaiser members in the Central Valley, so that they get a -- just a very -- you know, even if they don't read the report, they get a quick blurb on that.

And then the other thing is it might be good to end with an offer to meet with them and brief them further about the Program, if they're interested in learning more. And, you know, I think we could talk about the -- you know, whether we could follow up on that and potentially try to provide some briefings, because I think it might be a good time to do that.

CHAIRPERSON LUDERER: Any other comments, suggestions?

Sara.

MS. HOOVER: I just wanted to share a couple things that I just checked with Carol on. One is if you wanted to send it to like one other Panel member to help you edit it, that would be fine.

The other thing is, is I think there was interest expressed in sending it straight to the Governor and the Legislature, and that is fine. And you can -- she would suggest just CCing the heads of the agencies involved. So like the head of Cal/EPA, the head of CDPH, and, you know,

you could also CC the three department heads. So you could angle it that way, where you address the letter to the Governor and key members of the Legislature, that would be fine, and CC the appropriate agency and department heads.

CHAIRPERSON LUDERER: Is there any thoughts from the Panel about the two -- you know, the different approaches of addressing the letter, sending it directly to the Governor and the legislators versus the Department heads the way it was done last time?

PANEL MEMBER McKONE: The last time it was sent to the head of the Department --

CHAIRPERSON LUDERER: It was sent to the three departments. Sara clarified that. Not -- we only got the one, but they were the same letter sent to the different departments.

PANEL MEMBER McKONE: So the alternative would just be bypass and go right to the -- I mean, I don't know. I think if we really want to -- I mean, it will go to the department heads if we send it higher?

CHAIRPERSON LUDERER: You mean if we would CC it, certainly.

PANEL MEMBER McKONE: Yeah, CC it. But it basically -- I do think the point about drawing attention to the Program to the new administration -- it is a new

administration, the legislature always seems to be new. Because of term limits, there's so many new people. So, I mean, it might be nice to target it there just to keep drawing attention to the value of the Program, unless that's -- unless there's some political problems, but I don't see why it would.

CHAIRPERSON LUDERER: Are there any -- do any people have thoughts about specific legislators that you think would be receptive or would be good to let know.

PANEL MEMBER SOLOMON: Well, our Panel is appointed by the Governor and the Senate Pro Tem and the Speaker of the Assembly. So those three would probably be the primary addressees. And then CC's, I guess, could go to the secretary level at CalEPA and at HHS, as well as the Department heads.

And then I guess we'd need to check on whether there are specific legislators that would be particularly interested, but it seems like the heads of the Health Committees in the Senate and the Assembly, as well as the environment -- various environment committees would also be, so that would be four additional people.

CHAIRPERSON LUDERER: And I don't -- what about any of the legislators that were involved in really putting the bill forward, are they still in the Legislature or are they --

DR. DAS: (Shakes head.)

CHAIRPERSON LUDERER: They're all termed out?

DR. DAS: They're termed out.

CHAIRPERSON LUDERER: Okay. Any other discussions or recommendations?

All right.

PANEL MEMBER BRADMAN: I mean, I would agree that sending it to the administration and legislative level's also a good idea just to get it more widely distributed.

PANEL MEMBER McKONE: I mean, I'm just curious, I mean, none of us were appointed by the current Governor, right? Do we need to explain a bit about what -- I mean in theory Schwarzenegger had to know something about it or somebody did, because somebody on his staff made appointments. But does that -- do we need to sort of draw attention about this Program and make it clear that this Committee as -- maybe somewhere in the preamble just, in case they forgot, how this Panel was appointed.

PANEL MEMBER KAVANAUGH-LYNCH: I might suggest the Chairs of the Budget Committees also.

CHAIRPERSON LUDERER: Nice. Okay. Anymore discussion on that topic or we can move on to our final public comment period.

MS. DUNN: Dr. Luderer, were you going to take public comment on this item.

CHAIRPERSON LUDERER: Or comment period on that.

Yeah, then I guess we have another comment period after that.

Do we have any public comments on the present discussion.

Davis Baltz, Commonweal.

MR. BALTZ: Davis Baltz Commonweal.

I mean, in addition to all the good suggestions that have been put forward already that call attention to the significant achievements of the Program and the resourcefulness in accessing other funds, I think given the budget situation, if there's a skillful way to weave into this letter and/or report how biomonitoring can save public institutions valuable resources I think would be worth including.

Whether we can talk to CDC colleagues and get some specific examples, I know Dick Jackson used to talk about this case in Mississippi where they were illegally using an outdoor pesticide indoors. And because they could go in quickly and biomonitor and figure out exactly where it had been applied, and evacuate those who needed to be and calm the panic elsewhere, that one incident saved the State of Mississippi $50 million.

So the point is, is that biomonitoring has the potential to save California millions of dollars in

avoided healthcare costs, and environmental remediation. And it's hard to, you know, put a new line -- you know, put new resources in a budget when resources are scarce. But if the case can be made that it's going to save money down the line, it's worth mentioning.

And in addition, as was said in the letter to Dr. Horton in 2009, the enhanced lab capacity that the State has now offers the potential to, you know, be a revenue generator by taking on projects that previously it couldn't do because it didn't have the infrastructure.

So I think that could be worth adding to the letter. And if it's appropriate, and letters from community stakeholders would be helpful, I think several of those could be generated. Certainly, Commonweal would be willing to write one.

CHAIRPERSON LUDERER: Thank you.

Okay. We actually are moving on to another public comment period. We have at the end of the meeting now an open public comment period. There are actually 20 minutes allotted, but we're a little bit ahead of schedule, so we could potentially have a little bit longer public comment period, during which commentators can -- commenters can speak on any topic related to the California Environmental Contaminant Biomonitoring Committee Program.

And so do we have any Emails?

Okay. And do we have any speakers who are present who want to speak?

All right. We have a comment that was submitted via the web. This is from Vivian Parker, who says that she is a retired biologist.

Her comment, "Dear staff and advisory board members at OEHHA, I would like to ask you to consider biomonitoring for forestry herbicide uses in the rural counties of northern California.

"Each year approximately 200,000 pounds of pesticides, primarily herbicides, are applied to the watersheds and headwaters of streams, which supply 80 percent of California's drinking water." And this is data from the Department of Pesticide Regulation, CalEPA. "These chemicals are frequently applied aerially, where they can easily drift into streams and contaminate groundwater as well.

"Herbicides used for forestry are used in rates and concentrations that are toxic enough to kill hardwoods like oaks, and brush species, such as deer brush and manzanita. Several of these chemicals are known groundwater contaminants

(atrazine, 2,4-D, hexazinone, triclopyr, and imazapyr).

"The chemicals primarily used are glyphosate, hexazinone, 2,4-D, triclopyr BEE, imazapyr, and atrazine. Very little is known about the health effects of hexazinone, (a triazine-type herbicide) triclopyr or imazapyr.

"Residents living adjacent to industrial timberlands near Triangle Lake on the coast of Oregon west of Eugene were recently tested for atrazine and 2,4-D in their urine, and all 21 of the citizens tested were found positive.

"As result, the State Department of Agriculture has launched an investigation. You can read more at these web sites: www.registerguard.com. I believe that it is very likely that residents in many rural counties in California adjacent to industrial timber operations are also receiving regular exposure to forestry chemicals, and there's no oversight of this by any State regulators. There are also high cancer rates in many of these counties compared to other regions of the State.

"Counties with the highest forestry herbicide use are Humboldt, Shasta, Tuolumne, and these

also had the highest cancer rates in the State and in the years 2002 to 2006 data from the California State Cancer Registry.

"Thank you for all of your good work to protect our health and the environment".

And I'd like to thank the commenter for that input.

Do we have any other comments, from the Panel, from the public?

Dr. Solomon.

PANEL MEMBER SOLOMON: Yes. I spoke with Ms. Parker or Dr. Parker yesterday. And so, you know, her -- and I encouraged her to submit this comment to the entire Panel for discussion. And I also checked out the links that she included in her comment. Actually kind of interesting.

The small study in Oregon that she referred to was actually conducted by Dr. Dana Barr, who many of us know who used to be at CDC. And Dr. Barr pointed out that 2,4-D and atrazine are actually rarely found in the NHANES population. And so the fact that the levels were, you know, detected in this -- although it was a small study that, you know, in this population, it was kind of notable. And I thought so too.

And the other point that Ms. Parker -- or Dr.

Parker made. I'm not sure if she's a Ph.D. Biologist, but -- is that the triazine herbicides that are being used have actually been shifting. So atrazine, for example, has been used less and has been replaced to a significant degree by other triazine herbicides that are less well studied, less well understood.

And that comes back to some of the things that we've looked at as a Program before, where we're kind of looking at patterns of chemical use and how they're changing in the state of California.

And, you know, certainly some of the pesticides that she lists are already designated chemicals, because they're part of the NHANES program, 2,4-D and atrazine being examples, but some of the ones that she mentioned are not part of NHANES.

And so I would like to suggest that we put that list of chemicals in for potential -- you know, for evaluation as potential priorities and potential designated chemicals for our Program, and -- because we should know -- I realize, as a Committee, we've focused on the agricultural use of pesticides, and to some degree on the household uses, but forestry and right-of-way uses are also quite important.

CHAIRPERSON LUDERER: Any other comments from Panel members or from the public?

Sara.

MS. HOOVER: Yeah, I just wanted to mention that we separately received the comment, and we've already put these in the bin for screening, so we'll be starting on that.

CHAIRPERSON LUDERER: Okay. If we have no additional comments from the public or from the Panel Members, I guess we're finishing a little bit earlier here today.

And so what I want to do then is to remind everyone that there is going to be another Scientific Guidance Panel meeting held in Sacramento and that will be on November 10th. So that will be our next meeting.

And with that, then I would like to adjourn the meeting. Thank you all again for coming. Thank the staff for all their amazing work and all the exciting progress they shared with us today, and see you all November 10th.

Thank you.

(Thereupon the California Environmental Contaminant Biomonitoring Program, Scientific Guidance Panel meeting adjourned at 4:24 p.m.)

CERTIFICATE OF REPORTER

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

That I am a disinterested person herein; that the foregoing California Environmental Contamination Biomonitoring Program 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 26th day of July, 2011.

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