

MEETING
STATE OF CALIFORNIA
ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT
ENVIRONMENTAL CONTAMINANT BIOMONITORING PROGRAM
SCIENTIFIC GUIDANCE PANEL

THE CALIFORNIA ENDOWMENT
OAKLAND CONFERENCE CENTER
7TH FLOOR
1111 BROADWAY
OAKLAND, CALIFORNIA

THURSDAY, MARCH 27, 2014
10:00 A.M.

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

PANEL MEMBERS:

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

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

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

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

Julia Quint, Ph.D.

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

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY:

Dr. Gina Solomon, Deputy Secretary, Science and Health

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT:

Dr. George Alexeeff, Director

Dr. Lauren Zeise, Deputy Director, Scientific Affairs

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

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

Ms. Fran Kammerer, Staff Counsel

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

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

DEPARTMENT OF PUBLIC HEALTH:

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

Dr. Laura Fenster, Research Scientist

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

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

DEPARTMENT OF TOXIC SUBSTANCES CONTROL:

Dr. Myrto Petreas, Chief, Environmental Chemistry Branch

ALSO PRESENT:

Ms. Nancy Buermeyer, Breast Cancer Fund

Dr. Veena Singla, Natural Resources Defense Council

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

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1 P R O C E E D I N G S

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

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

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

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

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

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

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

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

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

1 Panel meeting was held on -- in Sacramento on November
2 10th, in 2013. At that meeting, the Panel heard about
3 program and laboratory updates. They unanimously voted to
4 recommend adding two classes of aroma chemicals, synthetic
5 polycyclic musks, and tetramethyl
6 acetyloctahydronaphthalenes to a list of designated
7 chemicals for Biomonitoring California.

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

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

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

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

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

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

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

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

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

1 And, Amy, if you could identify yourself.

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

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

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

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

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

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

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

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

17 So thank you, Dr. DiBartolomeis.

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

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

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

5 --o0o--

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

11 --o0o--

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

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

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

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

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

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

1 it's in very full force right now.

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

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

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

25 There is -- there are opportunities for

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

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

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

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

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

4 --o0o--

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

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

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

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

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

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

12 --o0o--

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

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

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

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

5 --o0o--

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

9 --o0o--

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

21 --o0o--

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

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

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

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

17 --o0o--

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

24 (Laughter.)

25 DR. DiBARTOLOMEIS: I'm not exactly sure what

1 else is -- what other reasons. So, let's see, and the --
2 this is interesting, the total enrolled mean age was 48,
3 and the sample mean age is 49. And if you recall from
4 Pilot BEST, it was significantly higher. I think it was
5 55, something like that.

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

11 --o0o--

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

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

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

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

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

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

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

1 key to the risk assessment for GDSP.

2 --o0o--

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

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

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

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

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

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

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

17 --o0o--

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

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

24 (Thereupon phone interference occurred.)

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

1 Hello.

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

7 (Laughter.)

8 --o0o--

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

10 (Thereupon phone interference occurred.)

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

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

21 --o0o--

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

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

5 (Thereupon phone interference occurred.)

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

8 (Thereupon phone interference occurred.)

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

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

12 (Thereupon phone interference occurred.)

13 (Laughter.)

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

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

22 --o0o--

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

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

7 --o0o--

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

17 --o0o--

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

21 (Thereupon phone interference occurred.)

22 MS. DUNN: Let's see.

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

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

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

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

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

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

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

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

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

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

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

7 Oliver.

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

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

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

25 PANEL MEMBER FIEHN: Of course.

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

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

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

25 PANEL MEMBER FIEHN: Thank you.

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

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

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

9 DR. PETREAS: I can answer that.

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

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

25 So this was like a snapshot of what could be

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

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

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

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

20 Oh, okay. Thanks.

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

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

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

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

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

14 PANEL MEMBER QUINT: Prenatal, the pregnant --

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

19 PANEL MEMBER QUINT: So all hospitals?

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

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

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

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

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

8 DR. WU: Yes, there's very good coverage. About
9 90 percent of newborns are screened.

10 PANEL MEMBER QUINT: Thank you.

11 ACTING CHAIRPERSON BRADMAN: Dr. Cranor.

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

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

1 heel stick of the newborn infant in a blood spot.

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

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

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

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

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

25 And then I just had a quick question on metals.

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

4 DR. GAJEK: Ryszard Gajek.

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

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

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

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

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

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

1 just --

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

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

11 PANEL MEMBER QUINT: Right.

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

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

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

21 PANEL MEMBER QUINT: Got it.

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

25 PANEL MEMBER QUINT: Okay. Thanks.

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

8 (Laughter.)

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

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

16 So thank you.

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

19 ACTING CHAIRPERSON BRADMAN: Is your microphone
20 on?

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

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

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

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

20 (Laughter.)

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

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

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

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

15 Dr. Fiehn.

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

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

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

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

11 MS. DUNN: Yes.

12 (Laughter.)

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

21 ACTING CHAIRPERSON BRADMAN: Dr. Quint.

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

1 that correct?

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

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

10 DR. PLUMMER: Yes.

11 PANEL MEMBER QUINT: Great.

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

15 Dr. Quintana.

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

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

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

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

13 ACTING CHAIRPERSON BRADMAN: Dr. Kavanaugh-Lynch.

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

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

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

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

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

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

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

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

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

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

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

14 ACTING CHAIRPERSON BRADMAN: Other questions?

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

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

25 (Laughter.)

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

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

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

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

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

18 (Laughter.)

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

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

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

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

9 Any ayes?

10 (Ayes.)

11 ACTING CHAIRPERSON BRADMAN: Any nays?

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

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

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

1 ACTING CHAIRPERSON BRADMAN: Thank you, Dr. She.

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

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

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

15 --o0o--

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

18 --o0o--

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

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

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

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

13 --o0o--

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

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

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

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

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

7 Thank you.

8 (Thereupon a discussion occurred off the record.)

9 MS. DUNN: Testing one, two.

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

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

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

16 (Laughter.)

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

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

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

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

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

4 MS. HOOVER: Give us one more minute.

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

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

9 MS. HOOVER: Okay.

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

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

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

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

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

3 --o0o--

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

11 --o0o--

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

19 --o0o--

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

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

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

5 --o0o--

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

11 --o0o--

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

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

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

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

15 --o0o--

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

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

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

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

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

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

3 And the other part that we use our own previous
4 database better experience, which, for example, I
5 mentioned, personally I like the database called ASES,
6 Automatic Structure Elucidation System, which includes
7 54,000 compounds. We licensed 2,800 compounds to NIST to
8 Dr. Stephen Stein, which is commercially used by people
9 who use GC-MS/EI database. So we build our own -- our own
10 database built it and the library search experience and
11 they're looking for further collaboration to expand this
12 database.

13 --o0o--

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

20 --o0o--

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

1 moment we need to develop a new strategy, but first this
2 700 in our library is our targeted unknowns.

3 --o0o--

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

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

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

19 --o0o--

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

23 --o0o--

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

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

8 --o0o--

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

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

18 --o0o--

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

1 compound that may also have difference.

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

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

12 --o0o--

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

23 Thank you.

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

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

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

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

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

20 PANEL MEMBER CRANOR: I'm sorry?

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

23 PANEL MEMBER CRANOR: Yes.

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

1 PANEL MEMBER CRANOR: Right. Right.

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

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

11 DR. SHE: Okay. Thank you.

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

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

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

21 --o0o--

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

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

6 --o0o--

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

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

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

23 We just completed analysis of maternal samples.
24 These are perinatal samples. These women were pregnant in
25 1959 to '66. And the bulk of the work so far has involved

1 the mother's samples. In addition, their adult daughters
2 had been contacted and 300 of them were sampled between
3 2011 and '12. And we also had these samples in our to-do
4 list.

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

14 --o0o--

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

25 --o0o--

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

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

13 --o0o--

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

20 And so far, we have blood samples from about
21 1,000 breast cancer cases and 1,400 controls from the
22 entire State. This is, of course, a breast cancer study,
23 but has other secondary objectives that help our work
24 here.

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

1 interesting demographics. I believe the median is around
2 65, but -- and the oldest one is 94. And the samples have
3 been analyzed for PCBs, PBDEs, perfluorinated chemicals,
4 thyroid hormones, and lipids.

5 --o0o--

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

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

21 --o0o--

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

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

11 --o0o--

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

18 They were sampled between 2010 and 12. We have
19 65 of them, and we have pairs of serum, cord blood, and
20 also breast milk. And we're completing the analysis for
21 PBDEs, pesticides, PCBs, perfluorinated chemicals, and
22 hydroxy-BDEs. We also have house dust from the homes, but
23 we haven't started that. We also have exposure assessment
24 questionnaires.

25 This is a study, which was partially funded by

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

6 --o0o--

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

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

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

--o0o--

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

--o0o--

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

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

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

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

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

6 --o0o--

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

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

20 So we're really very excited.

21 --o0o--

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

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

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

18 That's all I have to say.

19 ACTING CHAIRPERSON BRADMAN: Thank you, Dr.
20 Petreas.

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

1 So, Dr. Cranor.

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

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

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

17 PANEL MEMBER CRANOR: Okay.

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

22 PANEL MEMBER CRANOR: Very good.

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

1 PANEL MEMBER CRANOR: Very good.

2 ACTING CHAIRPERSON BRADMAN: Any other questions
3 or comments?

4 Dr. Fiehn.

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

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

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

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

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

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

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

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

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

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

1 things to look at.

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

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

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

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

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

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

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

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

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

18 (Laughter.)

19 ACTING CHAIRPERSON BRADMAN: Dr. Quint.

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

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

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

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

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

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

11 PANEL MEMBER QUINT: Good.

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

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

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

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

1 ACTING CHAIRPERSON BRADMAN: Anymore brief
2 questions?

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

8 Thank you.

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

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

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

1 information on those particular chemicals of concern.

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

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

13 (Laughter.)

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

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

1 eight months before that will be more generally public.

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

11 Thanks.

12 Dr. Cranor.

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

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

16 ACTING CHAIRPERSON BRADMAN: Okay.

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

23 DR. SHE: Maybe again Dr. Asa Bradman.

24 (Laughter.)

25 ACTING CHAIRPERSON BRADMAN: Okay. Just briefly.

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

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

13 So Dr. She.

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

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

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

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

23 (Laughter.)

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

1 assays, but no flame retardants.

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

6 (Laughter.)

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

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

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

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

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

14 ACTING CHAIRPERSON BRADMAN: Dr. Cranor.

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

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

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

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

5 ACTING CHAIRPERSON BRADMAN: Dr. Fiehn.

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

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

25 So this is definitely something that is of

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

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

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

1 go in.

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

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

14 (Laughter.)

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

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

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

4 All right. Thank you.

5 (Off record: 12:05 PM)

6 (Thereupon a lunch break was taken.)
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1 A F T E R N O O N S E S S I O N

2 (On record: 1:15 PM)

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

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

17 Thanks.

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

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

1 --o0o--

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

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

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

22 --o0o--

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

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

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

14 --o0o--

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

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

1 plans in this regard as yet.

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

4 Ryszard.

5 --o0o--

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

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

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

15 All right.

16 --o0o--

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

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

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

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

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

22 --o0o--

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

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

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

13 --o0o--

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

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

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

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

8 --o0o--

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

18 --o0o--

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

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

3 So this is already what I said.

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

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

18 All right. So thank you.

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

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

24 --o0o--

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

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

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

10 --o0o--

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

20 --o0o--

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

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

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

3 --o0o--

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

12 --o0o--

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

19 --o0o--

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

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

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

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

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

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

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

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

3 --o0o--

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

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

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

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

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

2 --o0o--

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

11 --o0o--

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

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

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

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

6 --o0o--

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

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

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

25 There was a study in Taiwan looking at resident

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

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

14 --o0o--

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

21 --o0o--

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

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

4 --o0o--

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

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

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

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

18 Dr. Quintana.

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

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

1 '98 as part of a trace element study. Yeah, that's all
2 I'm going to say.

3 ACTING CHAIRPERSON BRADMAN: Dr. Quint.

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

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

10 ACTING CHAIRPERSON BRADMAN: Dr. Fiehn.

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

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

1 toxicity of hexavalent chromium in the body.

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

10 ACTING CHAIRPERSON BRADMAN: Dr. Quint.

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

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

22 ACTING CHAIRPERSON BRADMAN: Could you identify
23 yourself?

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

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

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

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

9 ACTING CHAIRPERSON BRADMAN: Right.

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

17 ACTING CHAIRPERSON BRADMAN: Okay. Right.

18 Dr. Cranor.

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

25 ACTING CHAIRPERSON BRADMAN: So if we're done

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

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

7 MS. BUERMEYER: Thank you.

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

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

13 ACTING CHAIRPERSON BRADMAN: Thank you.

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

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

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

4 (Laughter.)

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

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

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

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

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

25 DR. GAJEK: One comment. Before collision cells

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

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

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

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

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

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

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

1 thing for chromium.

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

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

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

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

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

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

22 Sorry I was so long.

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

1 And so now we have time for Panel discussion.

2 Dr. Quintana.

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

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

14 PANEL MEMBER QUINTANA: Follow up.

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

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

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

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

7 ACTING CHAIRPERSON BRADMAN: Dr. Fiehn.

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

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

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

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

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

12 Just to --

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

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

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

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

8 MS. HOOVER: (Shakes head.)

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

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

25 And need to assess efficacy of public health

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

5 Adequacy of biospecimen samples.

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

11 Dr. Cranor.

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

17 Sara, can you help there?

18 MS. HOOVER: You're right.

19 PANEL MEMBER CRANOR: Okay.

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

23 PANEL MEMBER CRANOR: Right, as many as possible.

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

1 criteria at many different levels.

2 PANEL MEMBER CRANOR: Yes.

3 ACTING CHAIRPERSON BRADMAN: Any other comments?

4 Does anyone want to, or I will, make a motion?

5 How about I'll make a motion? So I, Dr. Bradman, want to

6 kind of submit the motion to the Panel that chromium be

7 included as a designated chemical in the California

8 Environmental Contaminant Biomonitoring Program.

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

10 (Laughter.)

11 ACTING CHAIRPERSON BRADMAN: Thank you.

12 Shall we have a vote?

13 (Laughter.)

14 PANEL MEMBER KAVANAUGH-LYNCH: Aye.

15 PANEL MEMBER FIEHN: Aye.

16 PANEL MEMBER QUINT: Aye.

17 ACTING CHAIRPERSON BRADMAN: Aye.

18 PANEL MEMBER QUINTANA: Aye.

19 PANEL MEMBER CRANOR: Aye.

20 ACTING CHAIRPERSON BRADMAN: Okay. So the Panel

21 has made a unanimous recommendation that chromium be

22 considered a designated chemical for the California

23 Environmental Contaminant Biomonitoring Program.

24 My next question is do we want to consider this

25 as a priority chemical or should we go on with the rest of

1 the presentation?

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

4 --o0o--

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

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

9 --o0o--

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

19 --o0o--

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

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

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

6 --o0o--

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

11 --o0o--

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

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

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

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

6 --o0o--

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

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

15 Dr. Cranor.

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

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

20 PANEL MEMBER CRANOR: Not by "and".

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

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

24 (Laughter.)

25 ACTING CHAIRPERSON BRADMAN: So anymore

1 clarifying questions?

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

5 Dr. Quintana.

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

9 MS. HOOVER: Yeah, beryllium and platinum.

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

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

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

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

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

9 ACTING CHAIRPERSON BRADMAN: Dr. Quint.

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

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

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

25 ACTING CHAIRPERSON BRADMAN: Dr. Fiehn.

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

12 (Laughter.)

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

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

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

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

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

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

1 (Laughter.)

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

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

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

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

22 MS. HOOVER: Yeah.

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

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

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

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

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

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

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

25 "The PBPK model also suggests that blood and

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

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

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

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

15 "Further, the exposure data summary states that
16 'CARB reports a State average ambient air concentration of
17 17.8 ng/m³ in 2012'. Such levels are well below even the
18 most stringent estimates of safe levels of inhalation
19 exposure for a lifetime".

20 And that standards -- a risk level proposed by
21 the Agency for Toxic Substances and Disease Registry was
22 set about 0.3 µg/m³. So there's some order of magnitude
23 differences -- several order of magnitude differences
24 between this and also a reference concentration proposed
25 by the Toxicology Excellence for Risk Assessment, TERA,

1 International Toxicity Estimates published a paper in 2011
2 proposing a manganese reference concentration of 2-7
3 $\mu\text{g}/\text{m}^3$, so two to three orders of magnitude higher.

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

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

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

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

25 So I think that completes then the public comment

1 phase of this discussion with regards to priority metals.

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

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

7 (Laughter.)

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

16 DR. GAJEK: (Nods head.)

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

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

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

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

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

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

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

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

25 And another comment. Recently, I listened to a

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

2 ACTING CHAIRPERSON BRADMAN: Bob Wright from
3 Mount Sinai.

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

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

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

1 really the purpose of your discussion here.

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

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

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

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

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

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

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

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

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

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

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

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

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

1 would vote to list them all.

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

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

12 (Laughter.)

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

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

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

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

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

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

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

15 ACTING CHAIRPERSON BRADMAN: Sure.

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

1 interpret data.

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

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

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

18 (Laughter.)

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

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

1 including manganese.

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

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

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

21 Dr. Quint.

22 PANEL MEMBER QUINT: Yeah. Julia Quint.

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

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

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

19 PANEL MEMBER FIEHN: Oliver Fiehn.

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

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

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

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

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

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

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

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

25 PANEL MEMBER QUINTANA: Cobalt?

1 PANEL MEMBER FIEHN: Cobalt is on there.

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

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

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

1 things.

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

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

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

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

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

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

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

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

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

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

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

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

25 DR. GAJEK: May I address?

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

3 PANEL MEMBER CRANOR: Two of us here.

4 ACTING CHAIRPERSON BRADMAN: Okay.

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

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

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

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

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

1 sure I have the correct list in front of me.

2 ACTING CHAIRPERSON BRADMAN: Sure.

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

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

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

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

1 selenium, arsenic metals, they are very difficult.
2 Ionization under plasma condition changes between 20 and
3 30 percent, so it limits the useful signal for these
4 metals. Mercury is also considered as the most difficult,
5 one of the most, manganese, chromium too. So I selected
6 these metals for purpose. I make my life more difficult,
7 not easier.

8 (Laughter.)

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

16 PANEL MEMBER FIEHN: I prefer one on one.

17 MS. HOOVER: Turn your mic on.

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

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

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

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

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

11 ACTING CHAIRPERSON BRADMAN: Cesium is Prop 65.

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

14 ACTING CHAIRPERSON BRADMAN: Right.

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

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

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

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

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

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

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

15 All right.

16 (Laughter.)

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

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

24 PANEL MEMBER CRANOR: I will second it.

25 ACTING CHAIRPERSON BRADMAN: Okay. So we have a

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

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

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

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

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

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

18 ACTING CHAIRPERSON BRADMAN: Yeah, I guess. Yeah.

19 PANEL MEMBER CRANOR: Treat it as a group.

20 ACTING CHAIRPERSON BRADMAN: Sure

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

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

1 mean --

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

4 PANEL MEMBER KAVANAUGH-LYNCH: Okay.

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

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

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

24 (Laughter.)

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

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

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

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

14 (Laughter.)

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

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

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

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

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

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

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

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

25 (Laughter.)

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

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

18 Is there anyone who'd like second that?

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

21 PANEL MEMBER FIEHN: I second.

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

24 (Laughter.)

25 ACTING CHAIRPERSON BRADMAN: So why don't we

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

3 PANEL MEMBER KAVANAUGH-LYNCH: Aye.

4 PANEL MEMBER FIEHN: Aye.

5 PANEL MEMBER QUINT: Aye.

6 ACTING CHAIRPERSON BRADMAN: Aye.

7 PANEL MEMBER QUINTANA: Aye.

8 PANEL MEMBER CRANOR: Aye.

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

18 Dr. Kavanaugh-Lynch.

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

22 ACTING CHAIRPERSON BRADMAN: Can I rephrase that?

23 PANEL MEMBER KAVANAUGH-LYNCH: Yes, please.

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

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

5 PANEL MEMBER KAVANAUGH-LYNCH: Yes, I would.

6 ACTING CHAIRPERSON BRADMAN: Would anyone like to
7 second that?

8 PANEL MEMBER QUINT: I'll second.

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

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

21 DIRECTOR ALEXEEFF: You didn't vote on that.

22 ACTING CHAIRPERSON BRADMAN: Oh, I'm sorry.

23 (Laughter.)

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

1 (Laughter.)

2 ACTING CHAIRPERSON BRADMAN: I am the Acting
3 Chair today.

4 (Laughter.)

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

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

9 PANEL MEMBER QUINTANA: Aye.

10 ACTING CHAIRPERSON BRADMAN: Yes.

11 PANEL MEMBER QUINT: What are we voting on?

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

14 PANEL MEMBER QUINTANA: Yes.

15 PANEL MEMBER FIEHN: Yes.

16 PANEL MEMBER KAVANAUGH-LYNCH: Yes.

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

20 PANEL MEMBER CRANOR: Did you say barium or
21 beryllium?

22 ACTING CHAIRPERSON BRADMAN: Beryllium.

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

1 manganese, molybdenum, thallium, tungsten, and uranium.

2 ACTING CHAIRPERSON BRADMAN: Correct.

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

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

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

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

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

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

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

1 15?

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

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

5 Thank you.

6 (Off record: 3:00 PM)

7 (Thereupon a recess was taken.)

8 (On record: 3:11 PM)

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

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

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

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

5 (Laughter.)

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

8 MS. HOOVER: Yes, I will.

9 ACTING CHAIRPERSON BRADMAN: Okay. Thank you.

10 MS. HOOVER: Yes, I will.

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

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

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

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

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

16 Dr. Sobus.

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

19 (Applause.)

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

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

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

16 --o0o--

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

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

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

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

12 --o0o--

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

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

1 computational toxicology, and then extramural research.

2 --o0o--

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

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

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

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

25 --o0o--

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

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

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

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

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

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

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

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

23 --o0o--

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

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

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

7 --o0o--

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

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

22 And we basically saw that in 1999 there was about
23 50 papers that appeared to be using the NHANES data. And
24 as you can see, there's been a very clear and sharp
25 increase over time, so that in 2012, there was over 400

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

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

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

16 --o0o--

17 DR. SOBUS: So the next question is what are
18 people doing with it? So when we aggregate the results
19 from this NHANES lit review, we found there was about
20 3,000 papers that appeared to be using the NHANES data.
21 Upon manual curation, we found that about 2,600 weren't
22 focusing on biomarkers at all. They were just looking at
23 nutrition or health endpoints. And only about ten percent
24 were actually focused on the chemical biomarker data.

25 So we further broke it down into applications of

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

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

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

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

25 So the bulk of these risk-based studies performed

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

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

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

1 some predictor of exposure.

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

8 So a fairly small percentage actually were, what
9 we called, exposure focused. The bulk were health
10 focused. So they were saying, this biomarker
11 concentration is predictive of this health endpoint. And
12 then when we further broke out that category to say, you
13 know, how are these health focused studies being
14 conducted, the very large, overwhelming majority, 116 out
15 120 studies were targeted in the sense they compared one
16 or a few chemicals with basically one endpoint. So very
17 targeted evaluations with *a priori* hypotheses being
18 tested.

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

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

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

4 --o0o--

5 DR. SOBUS: So I'll talk in depth about two case
6 studies and then briefly mention a few others. The first
7 case study that we focused on wanted to kind of look at
8 these association-based research endeavors. A colleague
9 of mine in NCEA, Krista Christensen, came up with the
10 observation that -- she was looking at the relationship
11 between phthalates and measures of body size, she was
12 getting different results in her epidemiological models,
13 and we wanted to comment on that.

14 So we put together this study. We've now
15 submitted a paper to Environment International. And the
16 title of the paper was, "Changes in epidemiologic
17 associations with different exposure metrics: A case
18 study of phthalate exposure associations with body mass
19 index and waist circumference."

20 So again, we kind of had this observation that
21 when you build these epidemiologic models, you have the
22 option to pick different exposure surrogates for a
23 particular biomarker. So, for example, if you have a
24 urine biomarker, you can do urinary concentration or
25 creatinine-adjusted concentration.

1 And we found that depending on which one you
2 pick, you get a different answer in your epi model. So
3 the question is which one is more right, or which one is
4 less wrong?

5 So ultimately, what we wanted to know with this
6 case study is, can we define and recommend best practices
7 for picking an exposure metric for any epi model?

8 So how did we go about doing that?

9 Well, the first thing we did was we looked at the
10 NHANES data and we calculated as many different exposure
11 metrics as we could for given phthalates. And then we
12 looked at the association between those exposure surrogate
13 levels and waist circumference and body mass index. So
14 that tells us the variation in results, but it doesn't
15 again tell us which one is most correct.

16 So we had to do a simulation experiment, where we
17 basically gave random exposures to the same NHANES
18 individuals and then looked for associations based on
19 those random exposures. And then we compared results of
20 the simulation to results of the actual NHANES analysis to
21 try and learn some lessons and then recommend best
22 practices.

23 --o0o--

24 DR. SOBUS: So it's a little hard to see, so I'll
25 walk you through it, but this is the results just using

1 the body mass index models. So we have here, for each of
2 these columns, the regression coefficients and standard
3 errors for five different exposure metrics. So we have
4 the first exposure metric is given in molar excretion
5 rate, so nanomoles per minute. The second is molar
6 concentration, nanomoles per ml. The third is
7 concentration, but including creatinine as an independent
8 variable in the model. This is something that's done
9 quite frequently now. The fourth is doing just a
10 creatinine-adjusted concentration measure. And the fifth
11 is doing a reconstructed intake that's adjusted for body
12 weight. So we have these five different exposure
13 surrogates that all originated from the same biomarker
14 level, and we did regressions for the different phthalates
15 with the outcome being the body mass index.

16 So if you look down for a given exposure metric,
17 you can see that the results are very consistent across
18 the different phthalates. For the excretion rate, we
19 basically have strong positive effect across the board.
20 When we move over to concentration, the effect is a little
21 bit stronger.

22 When we move over to the models that had
23 creatinine as an independent variable, the association is
24 a little bit weaker. Again, they're all in the positive
25 direction, but we're seeing some change in the

1 significance.

2 This gets interesting. When you move over to the
3 creatinine-adjusted value, the effects are no longer
4 significant at the 0.05 level. And then when we move all
5 the way over into the reconstructed daily intake,
6 extremely significant. So not a lot of difference in the
7 models across the different phthalates, but pretty large
8 differences, at least as far as interpretation goes, as
9 you move across the different exposure metrics.

10 So here we demonstrated the variability in the
11 results, given what you might find. I also want to point
12 out, this is only really a capability to do a lot of this
13 stuff in the '09 and '10 NHANES data, because they started
14 collecting full volumes of the void and reporting that.

15 And I'll show that in the next slide. You
16 couldn't do this type of analysis on earlier data, where
17 they didn't have full void volumes and the time of the
18 void.

19 --o0o--

20 DR. SOBUS: Okay. So I hope I've convinced you
21 that you have some variation in the results depending on
22 your exposure metric. So now we're trying to get at which
23 one may be the most correct, or at a minimum, the least
24 biased. So this is a complicated figure. I'll walk you
25 through it.

1 Essentially, again, what we tried to do was take
2 as much of that same NHANES data as we could, so the body
3 mass index, the waist circumference, and all the other
4 meta-data that you basically see up here in the red ovals.
5 But we threw away the biomarker concentrations, and
6 instead we started with the distribution of dietary
7 exposure that we got from a paper, Fromme et al. in 2007.
8 And we randomly assigned those dietary exposures to the
9 NHANES subjects.

10 So based on that random assignment, there should
11 be no association between the randomly assigned phthalate
12 exposure and the outcome of interest. I hope you can all
13 believe that. And we did test it, and there was no
14 association. So that was our starting point.

15 So basically what we're looking at is as you go
16 down the line and calculate the different exposure
17 metrics, if you see an association, it's demonstrating
18 that you've introduced bias, and the magnitude of the
19 regression coefficient says how much bias there is. And
20 ultimately that tells us which ones do we not want to
21 pick.

22 So this is how we did it, and I think this was
23 pretty clever. Again, we took the random intake and we
24 put it into a PBPK -- or a PK model, sorry, for DEHP that
25 published by Matt Lorber in 2010. We needed a couple

1 parameters to go into the model. We needed the weight,
2 which we could get from the NHANES, and we needed the time
3 of the void. Now, the NHANES will only give you three
4 different MEC sessions. They will not give you the
5 specific time of the void. So we took the MEC session and
6 we randomly selected a time for that subject, but we also
7 needed the time of the previous void.

8 We could get that by taking the urine volume and
9 the urine output that is now given in the 2009-2010
10 NHANES, and we calculated the time since the last void.
11 So we put that into the model. And all that combined
12 information right here allowed us to calculate the
13 chemical excretion for all the NHANES subjects. So it's a
14 totally made up value, but it should be independent of BMI
15 and waist circumference.

16 So that's really our first calculated exposure
17 metric, but we wanted to get the others. So when we took
18 chemical excretion and we coupled it with urine output,
19 again from the NHANES, we got chemical concentration.

20 When we took the excretion and coupled it with
21 creatinine excretion rate, we got the creatinine-adjusted
22 concentration. And when we coupled that with the
23 creatinine excretion model of Dave Mage from 2008, we
24 could predict the daily reconstructed intake. So through
25 this series of simulations, we were able to get the

1 original exposure metric, the truth as we assigned it, and
2 these four other exposure metrics that may or may not be
3 biased.

4 So the goal was then to run the same epi models
5 adjusting for the same parameters, age, sex, race,
6 ethnicity, poverty index to see if we got similar results
7 to what we saw with the actual NHANES data.

8 --o0o--

9 DR. SOBUS: And without showing a lot of
10 coefficients and P values, these are the results. So I'll
11 remind you what we saw with the NHANES data, we virtually
12 had no effect when we looked at creatinine-adjusted
13 concentrations. We had significant positive effects with
14 excretion rate and concentration values, and then we had
15 these really, really strong positive effects of the
16 reconstructed daily intake. And again, at the time, we
17 said we don't know which one is right.

18 Well, here's the simulation results. As
19 expected, there was no effect of random intake on BMI and
20 waist circumference. There was also no effect of
21 concentration and excretion rate on that outcome variable.
22 So from that, I would stop right here and say, you know,
23 concentration excretion rates are probably the least
24 biased exposure surrogates for this particular analysis.

25 But interestingly, we saw that the

1 creatinine-adjusted values, whether it be an independent
2 variable in the model or an outright adjustment in the
3 denominator, we saw significant negative effects between
4 the exposure surrogates and the outcomes of interest, that
5 completely demonstrates a negative bias that's been
6 introduced by the meta-data.

7 Then on the complete opposite side, we saw the
8 significant positive effect of the reconstructed daily
9 intake. Again, there should be no association, given that
10 there was no relationship between the true exposure and
11 the outcome variables of interest.

12 And I think what was most fascinating about this
13 is when you look at the order of these effects, you're
14 seeing the exact same order in the simulation results as
15 you're seeing down here in the NHANES results. The only
16 difference is these are shifted to the right. So that
17 tells me the fact that this has shifted to the right,
18 there could be something going on, some underlying
19 positive effect between the chemical exposure and the
20 outcome of interest.

21 But the fact that you're seeing this disparity
22 across the different exposure metrics being reflected in
23 the simulation, clearly indicates where some of this bias
24 is coming from. So we tried to, in the paper -- and I
25 won't get into it today -- kind of generalize this

1 procedure and recommend simpler procedures, so you don't
2 have to get into very difficult PBPK type simulations.
3 We're basically evaluating which exposure surrogate might
4 be the least biased and therefore most preferable for a
5 given epi study. So again, hopefully that paper will be
6 accepted in short order and something we can share with
7 everyone.

8 --o0o--

9 DR. SOBUS: Okay. So switching gears from the
10 association-based studies to risk-based studies. So
11 again, now we're talking about comparing biomarker
12 measurements from the NHANES or anything else to a
13 risk-based reference level, typically based on external
14 exposure.

15 So this was a study led by Joachim Pleil. He's
16 in our National Exposure Research Laboratory. This has
17 actually been published. This is the first paper that's
18 been published as part of our team. This was published in
19 the Journal of Toxicology and Environmental Health, Part A
20 fairly recently.

21 The title of this paper was, "Estimating lifetime
22 risk from spot biomarker data and intraclass correlation
23 coefficients". Now, we have shared this paper with group,
24 I believe. There's some math. So if anyone wants more
25 detail, they can certainly go to the paper and I'm happy

1 to talk to you about it afterwards.

2 But this was a really tricky problem.

3 Basically -- and this really focuses on nonpersistent
4 chemicals, but you've got these spot biomarker data in the
5 majority of studies, particularly the NHANES, where one
6 sample is collected from one person. Yet, the risk-based
7 reference levels are determined based on long-term
8 exposure, in most cases. So you've really got this apples
9 to oranges comparison. You know, how do you fairly
10 compare spot measurements to long-term average based
11 reference levels?

12 Ultimately, what we want to know here is what
13 percent of the population has long-term exposure above a
14 reference level? That's the ultimate science question
15 here. So to get at that, we first had to develop an
16 approach that would convert a distribution of spot samples
17 to a distribution of averages. Once we do that, we can
18 calculate population exceedance based on average biomarker
19 levels that would be above the reference level. And then
20 finally, we can develop a tool, so that people can
21 actually take information from places like NHANES or from
22 Biomonitoring California, plug in some statistical
23 parameters, and calculate these exceedance values for any
24 chemicals that they want. So hopefully, I can convince
25 you here that we've done that successfully.

--o0o--

DR. SOBUS: So to do this, we had to actually start with some real data. So this was hydroxypyrene data that I provided. It was 220 observations from a group of individuals with a known geometric mean and geometric standard deviation. And essentially, this was our starting point.

We wound up, and we detail this in the paper, kind of bootstrapping this, adding the number of observations, and then assigning repeated observations to individuals. And the goal was we wanted to manufacture different groupings of repeated observations, in order to calculate something called the intraclass correlation coefficient. And I'll give a little statistic tutorial.

--o0o--

DR. SOBUS: The intraclass correlation coefficient is essentially something called the between-subject variance component divided by the total variance. So the between-subject variance measures the difference in average biomarker levels across individuals in a population. The within-person variance component basically measures variability in repeated measurements for an individual over time. So the ICC has a possible range from zero to one.

Now, if there's no difference on average between

1 individuals in a population, we would say there's very
2 little between-subject variance, sigma square B is going
3 to be very near zero, and thus ICC is going to be very
4 near zero.

5 On the flip side, if everyone on average is very
6 different, but repeated measurements for an individual are
7 all very similar, we would say that sigma squared W is
8 near zero and thus ICC is near one. So what we did is we
9 took that original data set, and we bootstrapped it, and
10 we manufactured different groupings of the biomarker
11 measurements to generate all these different ICCs. And
12 then we built some mathematical models and used that data
13 for calibration. And again, I can't really get into that
14 today, but it's in the paper if you're interested.

15 --o0o--

16 DR. SOBUS: This was the output of all that
17 mathematics. These are five generated distributions of
18 average biomarker levels that are all based on that
19 original distribution of spot samples. And I'll first
20 draw your attention to the green line. It's a little bit
21 hard to see, but the green line represents the predicted
22 distribution under the condition where the ICC equals one.
23 So this says all of the variability in the biomarker
24 measurements are between subjects on average. There is no
25 variation within a subject.

1 In other words, if you were to take one
2 observation from one individual, that would be a very good
3 or perfect reflection of that person's average biomarker
4 level over time. So this is something we see more often
5 with persistent chemical biomarkers, not so much
6 nonpersistent chemical biomarkers. So we only show five
7 distributions here, but we can do this for any value of
8 ICC. And you can see that as ICC goes from 0.75 to 0.25,
9 or from 0.5 to 0.25 to zero, you have this tightening of
10 the distribution, such that more area is under this peak,
11 and less area is under the tail. So why is this
12 phenomenon important?

13 Well, let's say we have some biomonitoring
14 equivalent value out here. I will say, this is not a
15 value that we calculated. We just picked it out of
16 convenience to illustrate this point and the method.

17 So if we blowup the area to the right of this BE
18 level, we'll see something like this.

19 --o0o--

20 DR. SOBUS: So what we want to do here is
21 calculate the area under the curve to the right of the BE,
22 and that basically represents the percentage of the
23 population that generated the biomarker measurements that
24 would be in exceedance of a biomonitoring equivalent or
25 some value in biomarker space that's consistent with a

1 reference exposure level.

2 As you can see that when ICC equals zero, there's
3 no area under the curve. So, on average, no one would be
4 exceeding this BE. Perhaps in spot samples they would be
5 exceeding the BE, but not on average. And then as you go
6 up from ICC equals 0.25, 0.5, 0.75, and 1, you can see
7 there's more and more area under the curve.

8 So you can see here that ICC is really driving
9 what percentage of the population would be expected to
10 exceed the BE on average. So assuming that risk is
11 proportional to long-term exposure, we would say that in
12 this scenario up here, we have less risk and in this
13 scenario we have more risk.

14 So again, I'll turn your attention to the paper,
15 because I don't have time to get into it, but we did
16 generate a tool in Excel, where if you have a geometric
17 mean, a geometric standard deviation, an estimate of the
18 intraclass correlation coefficient, a number of repeated
19 observations, and some BE value or any other value of
20 interest, you can do these calculations for any chemical
21 that you want. And we're happy to share that tool with
22 anyone.

23 --o0o--

24 DR. SOBUS: Okay. So I took a little bit of time
25 on those. I just wanted to kind of briefly go through a

1 couple other kind of interesting case studies that we've
2 been performing. With respect to the association-based
3 studies, one of the things we found, particularly for the
4 nonpersistent chemicals, is there's very limited standards
5 for doing analyses and for reporting those analyses.

6 So if you go in and you target a study and look
7 for epi relationships between a nonpersistent chemical
8 biomarker and an outcome, there's very little guidance for
9 how to do that work, you know, how to evaluate the
10 biomarker itself, and how to report that.

11 So Judy LaKind put together a workshop made up of
12 experts in different fields, so epidemiologists,
13 analytical chemists, biomarker specialists. And we
14 basically came up with this proposal for assessing study
15 quality. And this is meant to be an instrument for
16 individuals reviewing research proposals, manuscript
17 submissions -- we're doing weight of evidence assessments.

18 And we called this instrument the,
19 "Biomonitoring, Environmental Epidemiology and Short-Lived
20 Chemicals Instrument." And again, the goal here is to
21 have something for doing systematic evaluations of these
22 association-based studies with the focus on the
23 nonpersistent chemical biomarkers.

24 So I'd be happy to follow up with anyone about
25 that, as would Judy, but this has been submitted to

1 Environment International.

2 The third challenge for association-based studies
3 that I'll talk about -- and I'll reference back to our
4 review slide, where we basically showed like 116 studies
5 did targeted association-based studies where four did
6 semi-supervised studies. We can probably be a little bit
7 more thoughtful about this than doing just one chemical
8 and outcome at a time, that there's limitations to using
9 the traditional regression-based models for doing multiple
10 testing, because you have to then adjust for multiple
11 testing to guard against false positives.

12 So a few of my colleagues in the health
13 laboratory -- or the Effects Laboratory, Shannon Bell and
14 Steve Edwards, came up with the idea of using frequent
15 itemset mining, a tool used in market-basket surveys, and
16 applying that to the NHANES data to basically look across
17 all environmental stressors and to look across all
18 outcomes, and then to prioritize association based on the
19 strength of association.

20 And this method actually gives you odd ratio
21 estimates. So they published the method, and they're
22 currently in the process of applying it to NHANES data
23 going back several years.

24 --o0o--

25 DR. SOBUS: The last study that I'll talk about

1 pertains to the risk-based evaluations. The distributions
2 I showed before in comparisons to the BE are an excellent
3 tool for looking at the population, what percentage of the
4 population would be exceeding BE, but we also had interest
5 in looking at individuals, and that's something that
6 that's been done before.

7 So it occurred to us that biomonitoring
8 equivalents are very useful pieces of information, but
9 there's not necessarily one biomarker concentration that
10 would be expected given exposure at a reference level.
11 These things vary over time, so there's likely many
12 biomarker concentrations that you could observe if you
13 randomly selected from an individual that had been exposed
14 at a reference level.

15 So the first thing we did for this study was
16 figure out how to generate a distribution of biomonitoring
17 equivalents. Then we statistically evaluated that
18 predicted distribution with observations of NHANES
19 biomarkers and we came up with a statistical
20 interpretation at the individual level, which was
21 basically the probability that any individual had been
22 exposed anywhere near the reference level.

23 So the goal of this evaluation was to basically
24 take the biomonitoring equivalent approach and start to
25 bring it to the individual level for interpretation. So

1 this is a paper that was submitted to Regulatory
2 Toxicology and Pharmacology. And we just were notified a
3 few days ago it has been conditionally accepted.

4 --o0o--

5 DR. SOBUS: Okay. How am I doing on time?

6 ACTING CHAIRPERSON BRADMAN: Ten more minutes.

7 DR. SOBUS: Great. So I'm going to completely
8 switch gears. I'm hoping this next bit of the talk is
9 relevant. So far, we've been focusing on project one,
10 which is, you know, trying to think of new ways to use
11 existing data.

12 This part is how do we go about collecting
13 samples in new ways, getting more information. And I hope
14 this is relevant. I heard about so many good studies that
15 you all are involved with in leading. I hope this is
16 relevant information to your work.

17 So about four or five years ago, we started
18 conducting this, what we call, the Exposure
19 Reconstruction, or Ex-R, Study. The goal here was to, A,
20 focus on urinary pyrethroid metabolites, but to really
21 carefully assess the variability in these biomarker levels
22 for non-occupationally exposed adults over a six-week
23 period of time.

24 We generated massive amounts of samples, as you
25 will see. And the ultimate goal was to use these massive

1 amounts of samples and data that we are generating to
2 accurately estimate exposure and absorbed doses using
3 mathematical exposure reconstruction approaches.

4 --o0o--

5 DR. SOBUS: So this was a fairly large team. The
6 principal investigator was Marsha Morgan at EPA. I was a
7 part of the field team and the analytical team and we were
8 in the field for, I believe, a couple years. But again, a
9 fairly large effort that spanned a fairly decent chunk of
10 time.

11 --o0o--

12 DR. SOBUS: So some specific study info. This
13 study took place both at the EPA Human Studies Facility in
14 Chapel Hill, North Carolina, in addition to participant's
15 homes, which had to be within a 40-mile radius of the
16 facility.

17 We recruited 50 adult subjects ages 18 to 50, and
18 each participant was actively engaged in the study for a
19 six-week monitoring period. Specifically, they provided
20 samples and filled out questionnaires during weeks one,
21 two, and six of the study.

22 So from them, we had them fill out food diaries,
23 activity diaries, and pesticide use diaries. We collected
24 duplicate solid food samples, a drinking water sample, a
25 surface wipe samples, dust, and many, many, many urine

1 samples.

2 The primary sample analysis has focused on
3 pyrethroids and metabolites, but this has been expanded to
4 include other chemicals through partnerships with CDC and
5 through internal analyses. The field study duration
6 started November 2009, ended May 2011, and we're just now
7 starting to see some of the chemical biomarker data coming
8 back in.

9 --o0o--

10 DR. SOBUS: So I want to give you a handle on
11 basically what a typical week looked like for the
12 participants. On days one and two, we got duplicate diets
13 of the breakfast, lunch, and dinner. Starting at the end
14 of day one with the bedtime void, we got -- and these are
15 all full voids, full volumes. We got the bedtime void,
16 every void on day two through the first morning void on
17 day three, and then we repeated that procedure at the end
18 of the week.

19 We got a surface wipe sample every day four. We
20 got one vacuum dust sample only in week six. And we got
21 one drinking water sample only in week six. But we had
22 diary information for both food intake and activities
23 virtually for every day that we did sampling with the
24 exception of days where subjects would come to the clinic
25 to swap out kits.

--o0o--

DR. SOBUS: So when I say kits, I mean these. We basically wanted to do an observational study where people went on about their business. We had them give us information about what they were doing and we had them provide us with lots and lots of samples. So we had to figure out a fairly clever way to allow them to collect samples, to store the samples, and bring them back to us at refrigeration temperatures.

So we came across these portable thermoelectric coolers that could really contain a fair amount of samples as you will see. And we basically each -- each thermoelectric cooler represented a daily kit. And we would give instructions, and diaries, and checklists, have everything color coded and bar coded, and make sure that the subject had everything they needed in that cooler. And they could plug it into the car or plug it into the wall and make sure all the sample stayed cool at all times.

--o0o--

DR. SOBUS: So one of the really clever things that we did, I think, was we put these very inexpensive, very small temperature loggers that plug into the USB drive of the computer, and we put these in each of the kits. And that allowed us to do three things.

1 Number one, it allowed us to track cooler
2 performance. So if we had -- some coolers just ran colder
3 than others. And obviously, you want to keep samples,
4 particularly biological samples as cool as possible. So
5 if we had a sampling container that wasn't functioning
6 well, we could easily track that and move it out of the
7 rotation and bring in something else.

8 Second, as we start to get our pyrethroid data
9 back in, it will be very interesting to look at the
10 temperature data and compare it to the residues to make
11 sure we didn't have -- or we have no evidence of
12 degradation.

13 Because this study went over, you know, several
14 seasons, the coolers perform a little bit differently in a
15 winter month, as they would compared to a summer month,
16 because they bring the temperature down so much below
17 ambient. So that's definitely a consideration.

18 And then the third point is monitoring subject
19 compliance. No matter how often we told subjects to take
20 the coolers home and to plug them in and keep them plugged
21 in, they would always go home, put it in the corner, and
22 not plug it until they collected their first sample. And
23 when they'd come back to the clinic and we would plug this
24 in, we'd say, "You didn't follow directions and we can see
25 that".

1 So it was a great way to have reinforcement to
2 make sure the subjects were following directions. And
3 they kind of had an aha moment of oh you are watching me.

4 (Laughter.)

5 ACTING CHAIRPERSON BRADMAN: Five more minutes.

6 --o0o--

7 DR. SOBUS: Yep. So I'll cruise through these
8 last slides. These are just some pictures of what the
9 human studies facility work looked like. We had to
10 assemble hundreds of these kits, but we did it very
11 successfully. We would store all the kits in groups.
12 Each subject would take two coolers with them for the
13 beginning of the week and then two coolers with them for
14 the end of the week. We never had any complaints about
15 that being too cumbersome.

16 We did -- two of us would handle the training
17 sessions, about an hour and a half per subject, and we
18 would walk them through the daily coolers. And then when
19 subjects would come back in -- I think this was another
20 really clever thing we did. Again, we're getting full
21 volumes of literally thousands of urine samples, and we
22 have to get an accurate estimation of the volume. The
23 last thing you want to do is to be doing graduated
24 cylinder measurements of those of urine samples for
25 various reasons.

1 (Laughter.)

2 DR. SOBUS: So when I was told that I would
3 probably be doing that as we were checking in the
4 subjects, I came up with this little thing that I named
5 the Sobusizer, which was plastic sleeve that we put
6 etchings on with different volumes. And we could just
7 slide it over the sampling container, read off the
8 measurements. We did some experiments. This had great
9 precision, great accuracy. It worked phenomenally well.

10 So for anybody doing -- again, I'm a huge
11 advocate of getting the full sample, getting the time of
12 the void, and this is a fantastic way to very quickly and
13 accurately and cleanly get the volume.

14 --o0o--

15 DR. SOBUS: Again, I'm just going to fly through
16 these. In addition to the trainings, we gave beautiful
17 instruction manuals to the subjects that they were located
18 in the corner pockets of these coolers. We would tell
19 them every day before you go bed read the instructions for
20 the next day, because we don't want you waking up, doing
21 your first morning void, and then looking at your
22 instructions and saying, "Ah, I was supposed to get that".

23 So we gave them very clear directions, showed
24 them how to fill out the diaries, showed them how to
25 collect their samples, made sure that they filled out the

1 time of the samples and the corresponding time on the
2 activity diaries.

3 --o0o--

4 DR. SOBUS: This is an important point. Everyone
5 I've talked to -- not everyone, but most of the people
6 I've talked to, including NHANES, uses 500 ml containers
7 for doing urine sampling. We tested that and it wasn't
8 enough. So we used one liter containers. And I'll show
9 you some statistics in a minute, but we could fit 11 one
10 liter containers in these thermal electric coolers in
11 addition to the duplicate food samples.

12 So these things had great capacity, but it's just
13 like carrying around a piece of luggage. So this really
14 did work fantastically.

15 --o0o--

16 DR. SOBUS: This is just a quick example of the
17 checklist that we'd have subjects check off at the end of
18 every day to make sure that they didn't miss anything.

19 --o0o--

20 DR. SOBUS: I wanted to give some statistics on
21 how successful we were. There was a total of about 4,000
22 samples that could have been collected. We calculated
23 about 2,600 events that actually happened during the
24 collection periods. We had a 97 percent completion rate
25 in terms of getting the samples. Only three percent were

1 acknowledged missing. We had very, very few partial
2 voids, which is a little bit unbelievable. And because
3 that's so unbelievable, I said I need to go make sure that
4 this is truth. So I came up with a little basically
5 five-step methodology for evaluating if a subject was
6 lying to us about missing a sample or having a partial
7 void.

8 Because if they missed a sample or had a partial
9 void, it's a big deal. You're going to underestimate the
10 day's urine output, you're going to underestimate the
11 day's chemical excretion and ultimately you're going to
12 underestimate exposure. And that's not something we want
13 to do.

14 So the visual is a lot more easy than the
15 statistics.

16 --o0o--

17 DR. SOBUS: There's a statistical component of
18 this that I did. But you can see here we had a subject
19 that was -- these were all 24-hour periods. There's six
20 of them. You can see there were clearly between 1 and 10
21 ml per minute across the board. And they had this one
22 observation that was just way out, close to 0.1 ml per
23 minute. I confirmed it as an outlier with a normal
24 probability plot. Again, I did some statistical
25 evaluations and I looked at creatinine specific gravity.

1 And through that, I only found about 17 samples that I
2 believed to be suspicious.

3 --o0o--

4 DR. SOBUS: This is just for your reference.
5 Again, like I said, 500 ml container, we would have lost
6 somewhere above, I don't know, the 85th percentile. We
7 had lots of people -- or lots of samples, I should say,
8 that produced samples in excess of 500 ml. So if you use
9 a 500 ml container, again you're going to underestimate
10 urine output and ultimately underestimate exposure.

11 So that's something to consider if you're doing
12 full voids, which again I'm a huge advocate for. And this
13 is just to give you an idea of the range of void events
14 over a day or a 24-hour period. We had an average of
15 about seven to eight, but as few as three and as many as
16 14. So there's certainly some planning. But again, our
17 coolers allowed as many as 11 in a particular 24-hour
18 period, so we had very little loss of sample due to an
19 extreme number of events.

20 --o0o--

21 DR. SOBUS: So we had some really good keys to
22 success. Again, the training sessions went extremely
23 well. We would give subjects these ad hoc refreshers as
24 needed, especially when they came back for week six
25 sampling. The instruction manuals were absolutely a huge

1 hit.

2 Let's see. You know, QA check points everywhere.
3 We're trying to get more into the technology benefits and
4 allowing that to really enhance our studies. So where we
5 put bar codes on everything and did direct data uploads
6 and did temperature loggers, I think going forward we're
7 really going to try and implement some of these
8 technologies. And I would really recommend them for
9 others.

10 --o0o--

11 DR. SOBUS: Electronic diaries rather than hard
12 copy diaries, especially with reminder alarms, because we
13 saw many incidents where subjects would come in with an
14 empty diary. And you'd see that look of panic on their
15 face, and they would say, "Oh, darn it. I'm going to go
16 fill out my diary".

17 So I think to the extent that we can use tablet
18 and smart phones and have reminder alarms for electronic
19 diaries, that would be huge. Using smart phones to do bar
20 code scans for consumer products and the sampling
21 containers would be extremely efficient, and ultimately
22 taking advantage of web applications for, you know, meal
23 snaps, seeing how many calories are in a meal, you know,
24 how much activity, how many miles walked per day, that
25 kind of thing, would be really, really advantageous.

--o0o--

DR. SOBUS: And just to drive some things home. I hope I've helped convince people that there's really cool innovative ways to go about examining existing data and collecting new data as we go forward. And I think the collecting new data thing, as I heard earlier today, is going to be really, really interesting. And I think we really want to participate in some of this untargeted analysis, because there's many, many chemicals that we're not considering as biomarkers right now, and we really have to do evaluations on thousands of chemicals.

So to be thinking about how we can enhance biomonitoring to be evaluating models that make predictions with respect to exposure and toxicity for lists of thousands of chemicals, that will become really, really critical.

So thank you so much for your attention. I hope this resonates with some people and hopefully it will be meaningful and the start of further discussion.

Thank you.

(Applause.)

ACTING CHAIRPERSON BRADMAN: So thank you, Dr. Sobus, for that very interesting presentation. Definitely relevant to the work of the Biomonitoring Program and many others of us who are collecting these kind of

1 measurements. So we have some time right now for Panel
2 questions, and that will be followed by opportunities for
3 public comment. So if there are any thoughts and
4 questions among the Panel?

5 Dr. Quintana.

6 PANEL MEMBER QUINTANA: Hi. Thank you for that
7 whirlwind tour. I had some comments and I don't want
8 things to sound negative, because I realize if I start --
9 it's not like I'm criticizing everything you're doing, I'm
10 not. But I had two comments. One was on the
11 biomonitoring equivalents. And I thought you were going
12 to show that graph with the hazard index and the ranges
13 that was in one of the materials you submitted. And this
14 is where you are picking the amount of biological
15 contaminant in the body that would correspond to the
16 regulatory levels, is that correct?

17 DR. SOBUS: I'm not sure if you're referring to
18 something I submitted or something that was submitted by
19 Summit Toxicology.

20 PANEL MEMBER QUINTANA: Or something that was
21 submitted -- a public comment, sorry.

22 DR. SOBUS: Right.

23 PANEL MEMBER QUINTANA: But didn't you -- but
24 you're not involved in generating the biomonitoring
25 equivalents, just in critiquing them, is that what you're

1 saying?

2 DR. SOBUS: I don't know if I'd say critiquing
3 them. Perhaps thinking of innovative ways to help enhance
4 them -- or help enhance the interpretation against them.

5 PANEL MEMBER QUINTANA: Okay.

6 ACTING CHAIRPERSON BRADMAN: I think you're
7 referring to slide 16, where he talked about kind of a
8 theoretical biomonitoring equivalent as a cutoff to
9 evaluate. And I think that was just used as a simulation.

10 DR. SOBUS: Correct.

11 ACTING CHAIRPERSON BRADMAN: That wasn't an
12 actual biomonitoring equivalent.

13 PANEL MEMBER QUINTANA: No, I agree. I guess
14 my -- I have two comments on that slide going back to
15 slide 16, which was the -- you said what percent of the
16 population would exceed a value. And if you had a very
17 stable biomarker, you're saying a single measurement would
18 be more accurate than if it was -- it had variability,
19 then you have fewer exceedances. But I think this is true
20 given your assumption that it's the long-term exposure
21 that matters, but I --

22 DR. SOBUS: Correct.

23 PANEL MEMBER QUINTANA: -- do want to say, there
24 are many situations, and pregnancy is one, where -- and
25 I'm thinking specifically of the atrazine controversy in

1 the water, where they -- I believe they were averaging the
2 level of atrazine to compare to a standard, but in fact
3 there were these events with very high atrazine
4 concentrations. And so -- and if you were pregnant and
5 you drank the water that day, that might have a
6 significant effect on your baby. And it was really
7 related to peak events and not the average level of
8 atrazine.

9 DR. SOBUS: Absolutely.

10 PANEL MEMBER QUINTANA: And so I just think if
11 you make these models, it's important to emphasize what
12 the underlying assumptions are --

13 DR. SOBUS: Right. And at this point --

14 PANEL MEMBER QUINTANA: -- which may not be
15 appropriate for some outpoints.

16 DR. SOBUS: I think I made the point today that,
17 you know, this is really looking at where risk is being
18 evaluated based on long-term term exposure. And we
19 certainly make a point of that in the paper, but that's an
20 absolutely excellent point.

21 PANEL MEMBER QUINTANA: And I also think that the
22 idea of biomonitoring equivalents is really useful, but I
23 think getting back to Dr. Quint's comment earlier about
24 the OSHA PEL for chromium, where people might start taking
25 standards as meaning it's okay, as opposed to this is a

1 number that was come up with with a huge amount of
2 controversy. For example, arsenic in drinking water, some
3 people wanted it lower, you know, some higher. And so
4 that level might be used as a hazard index, but it was not
5 necessarily the health-based level.

6 DR. SOBUS: Sure. We actually have a discussion
7 of that in the paper too, in that one of the reasons that
8 we kind of artificially chose a biomonitoring equivalent
9 level is that you can pick any level of interest.

10 The goal here is to say we've been limited, in
11 that when you compare a distribution of spots to a BE,
12 you're basically using only the median value, and you're
13 not really focusing on the upper percentile of the
14 distribution, or, if you are, you're kind of -- you're
15 lacking confidence in what that means. So this is a
16 mechanism to make it an apples to apples comparison.

17 The value you choose for the BE is up to you, so
18 if you don't want to take into account uncertainty
19 factors, or if you want to use a PEL instead, I mean,
20 that's all completely appropriate. It's the mathematics
21 of going from the distribution of spots to a distribution
22 of averages, and then interpreting that based on average
23 exposures. And again, if you're talking about peak events
24 being related to toxicity, this isn't the method for you,
25 but I mean your points are absolutely on point.

1 PANEL MEMBER QUINTANA: And the last -- very last
2 comment -- sorry -- is that when you started out, you're
3 talking about interpreting your N values, for example.
4 And you had daily intake in your model for phthalates, for
5 example --

6 DR. SOBUS: Right.

7 PANEL MEMBER QUINTANA: -- but there's behavior
8 variability that goes into that as well. For example,
9 cotinine has a short half-life, but it's a pretty accurate
10 marker of cigarette smoke exposure, because the behavior
11 is so stable. Whereas, something else with a short
12 half-life that you're only exposed to once a week at the
13 gas station might be more variable, but those two
14 situations might look the same in your model, because
15 you're just looking at a certain -- you know, you're not
16 looking at the behavior variability on top of the other
17 stuff as well, I guess.

18 DR. SOBUS: So I'm not sure, are we talking about
19 the risk-based or --

20 PANEL MEMBER QUINTANA: I can't remember.

21 DR. SOBUS: -- or the association-based
22 approaches?

23 PANEL MEMBER QUINTANA: I'm talking about the
24 slide -- you showed a lot of slides. Way down to slide --
25 the very beginning of your talk. I can't see without my

1 glasses. I'm just saying is that there's a lot of things
2 that go into making up variability, which can't always be
3 captured with just starting with a PBPK model on a daily
4 intake.

5 DR. SOBUS: Oh, absolutely. And that's why,
6 again, I think -- I tried to separate the talk into
7 existing data being so much of spot measurements, and
8 having no idea how to understand variability with spot
9 measurements to going forward in the studies that we're
10 doing collecting lots and lots and lots of samples to
11 understand variability and sources of the variability, be
12 it going to the gas station or something else.

13 So that's why I said project one is we're using
14 what we've got and we're trying to use it to the best of
15 our ability. Project two is how do we be clever about
16 going out and getting the information that we need. So I
17 agree with you 100 percent.

18 PANEL MEMBER QUINTANA: Sorry for such a long
19 comment.

20 ACTING CHAIRPERSON BRADMAN: Any other questions
21 by the Panel for Dr. Sobus?

22 I have a question -- kind of a technical question
23 going back to slide 16, and the points leading up to that.
24 In terms of the -- you must -- to get an ICC, you have to
25 have some repeat samples. And I'm curious, have you

1 looked at in terms of the length of time between the
2 samples and how long that should be depending on the
3 estimated half-life of the compound?

4 DR. SOBUS: We had -- our team had a tremendous
5 amount of discussion about this, and absolutely, the
6 length of time, the population of interest. What we found
7 to be extremely important, and we describe in the paper I
8 skipped over today, is the number of repeats that you
9 have. You have a lot more confidence in your variance
10 components in your ICC given that you have more repeated
11 observations.

12 ACTING CHAIRPERSON BRADMAN: Exactly.

13 DR. SOBUS: And then we've also talked about if
14 ICCs are collected or based on repeated measurements over
15 a week, how does that pertain to a month, or a year, or
16 ten years? So these are all fantastic questions.

17 So the goal with this paper was just to put out a
18 methodology that says given that you know something about
19 it, can you do it?

20 Now, what we're doing is going out and getting
21 that data and doing it for more chemicals.

22 ACTING CHAIRPERSON BRADMAN: It doesn't look like
23 we have anymore comments. I just want to reiterate that
24 was a fascinating presentation and I think really
25 addresses some of the kind of core issues in exposure

1 assessment and biomonitoring that face a lot of us these
2 days, particularly for nonpersistent compounds, which are
3 such a challenge. Urine is such an easy media to take
4 measurements in, but how to use that is challenging, and
5 it's great to see your group addressing those questions.

6 So I think that's it.

7 Thank you.

8 DR. SOBUS: Thank you so much.

9 ACTING CHAIRPERSON BRADMAN: At this point, we
10 have some time for public comment related to this previous
11 presentation session. And are there any public comments
12 in the group here?

13 MS. DUNN: None.

14 ACTING CHAIRPERSON BRADMAN: No. Okay.

15 Then we have one comment that was submitted last
16 night by Lesa Aylward from the Summit Toxicology Group.
17 They've talked to us before, and I'm going to read some
18 highlights from their letter, which is perhaps related to
19 some of the early conversation. So this is -- again, this
20 is from Sean Hays -- Dr. Hays and Dr. Aylward from Summit
21 Toxicology.

22 "Dear distinguished Panelists...", with respect
23 to interpretation to biomonitoring data, "...Since we,
24 (Lesa Aylward specifically), presented to the Science
25 Guidance Panel in March of 2011, we've made significant

1 progress in developing biomonitoring equivalents as a tool
2 for interpreting human biomonitoring data. The
3 biomonitoring equivalents allow interpretation of
4 population-based biomonitoring levels and allows an
5 assessment of the margins of safety and/or hazard
6 quotients on a chemical-specific basis. Comparing MOSs,
7 margins of safety, and/or hazard quotients across
8 chemicals also allows a relative ranking that can serve as
9 a very powerful tool to allow public health agencies to
10 prioritize which chemicals pose the greatest threat to
11 public health amongst the population.

12 "We encourage the Scientific Guidance Panel and
13 the Biomonitoring California staff to utilize
14 biomonitoring equivalents and/or other such approaches to
15 interpreting biomonitoring data in a public health risk
16 context. While the biomonitoring equivalent values are
17 simply an initial screening tool, they do provide some
18 initial insight into the question of, 'what do the
19 measured biomarker levels mean?'"

20 I should mention there's a footnote here that,
21 "The biomonitoring equivalent is defined as the
22 concentration of a chemical, or metabolite, in blood or
23 urine that is consistent with an established tolerable
24 exposure guideline, such as reference dose, tolerable
25 daily intake, et cetera."

1 And again, that was signed by Sean Hays and Lesa
2 Aylward. And there's a little bit more length in here
3 that I didn't take the time to read today, because we're
4 constrained. But again, this comment is published on the
5 Biomonitoring website. And there's also some related
6 supporting information, including papers and other
7 literature.

8 So we now have some time for Panel discussion
9 related to this previous discussion, then we will have
10 time for open comment on anything related to today and the
11 Biomonitoring Program, and then we'll have a wrap-up and
12 announcement.

13 So I know I have some comments with respect to
14 this recent public comment. But I'm wondering if there's
15 any other input or comments from the Panel on anything
16 we've heard in the last presentation?

17 Dr. Fiehn.

18 PANEL MEMBER FIEHN: Okay. So I couldn't follow
19 everything the presenter said, and -- but I wondered when
20 you did your modelings, did I perceive this correctly that
21 you said if you do the creatinine adjustments, you
22 introduce bias? Is that, shortly, what I understood
23 correctly, when I have to go home?

24 DR. SOBUS: Is this on? Can you hear me? Is
25 this -- for that association-based study, that is not a

1 universal truth. What we were hoping to get from that
2 simulation was basically a procedure for going about
3 identifying bias.

4 So the result from that particular study, where
5 we were looking at body mass index and waist circumference
6 as the outcome variable, creatinine-introduced bias. And
7 that is because creatinine excretion is a function of body
8 size. So if a different outcome that was independent of
9 creatinine were being considered, creatinine may be a very
10 good tool for correcting for urine output.

11 So the goal of that wasn't to say this is good,
12 this is bad, it was to say you need to think about it and
13 this is how you should go about thinking about it. So we
14 try and detail, you know, kind of guidance for -- not
15 doing a full-blown simulation obviously in every example,
16 but some steps you can take to try and identify which
17 would be the best to use.

18 PANEL MEMBER FIEHN: That makes more sense.

19 ACTING CHAIRPERSON BRADMAN: But I think
20 though -- I guess we're going to go back to your
21 presentation, and a question. From slide 11, I think
22 there was an implication there that the
23 creatinine-adjusted value would be the least biased
24 predictor, if, in fact, there was a relationship -- it
25 would be the least biased exposure metric, if, in fact,

1 there was a relationship between the exposure and the
2 outcome in this case.

3 DR. SOBUS: So I believe you're referring to this
4 slide. So what I wanted to communicate with this slide
5 was in the simulation results in that middle category
6 where you see no effect --

7 ACTING CHAIRPERSON BRADMAN: Right.

8 DR. SOBUS: -- those would be the exposure
9 surrogates that were not associated with bias.

10 ACTING CHAIRPERSON BRADMAN: Correct.

11 DR. SOBUS: And that is because the meta-data
12 that went into producing concentration, and that value
13 being urine output, and excretion rate, that being time
14 between voids, are independent of body size. That's why
15 we had no introduced bias in those associations. The
16 negative effect says there was a significant negative
17 association.

18 ACTING CHAIRPERSON BRADMAN: Right. I'm sorry.
19 I misspoke. I meant the random -- yeah, the excretion
20 rate.

21 DR. SOBUS: Okay.

22 ACTING CHAIRPERSON BRADMAN: So based on this --
23 on your simulation result, you would say that the
24 excretion rate was probably the best -- the least biased
25 predictor of the outcome in this analysis?

1 DR. SOBUS: Yeah. You know, me personally, my
2 default would be excretion rate. It won't always be the
3 best. But based on my observations, it's something that I
4 would typically start with and then think about other
5 things. I was -- I wasn't surprised to see the
6 concentration had no bias. But for this analysis,
7 concentration and excretion rate performed equally well.

8 ACTING CHAIRPERSON BRADMAN: All right. Okay.
9 Thanks.

10 Well, I guess in terms of Panel discussion then I
11 have one comment in response to the public comment and
12 letter submitted by Summit Toxicology. First, I want to
13 say I think the biomonitoring equivalent field and
14 approach to evaluating measurements I think is very
15 valuable. And I think it's a great contribution to the
16 science and really gives us ways to think about how to
17 interpret these results.

18 But we've talked about this before as a Panel,
19 and, you know, as she recommended to us, we encouraged the
20 SGP and the Biomonitoring California staff to utilize
21 biomonitoring equivalents and/or other such approaches for
22 interpreting biomonitoring data in a public health risk
23 context.

24 In the past, we've had discussions on the Panel
25 around that issue. And, in general, we, or at least I,

1 have felt strongly that the Biomonitoring Program should
2 not get involved in risk assessment and risk evaluation.
3 That because of the complexities and challenges of that,
4 really the goals of the Program should be to produce good
5 information on exposures and measurements in matrices.
6 And that the risk interpretation, while important to do,
7 should occur in some other context, so the Biomonitoring
8 Program itself won't be bogged down in the debates and
9 often political controversies that come over the risk
10 assessments and risk management.

11 I just want to respond to that, but I still very
12 much respect the work being done by Summit Toxicology on
13 these issues.

14 Sure. Dr. Quintana.

15 PANEL MEMBER QUINTANA: Hi. Jenny Quintana.

16 Will, first of all, I guess I'll make the comment
17 to Dr. Sobus that I got mixed up. It was -- this
18 submitted document -- yeah, one of my comments was
19 addressing was stuck to his presentation, and I thought --
20 I got mixed up it was his too. So that being said, I want
21 to clarify that one of my comments wasn't addressed to
22 him. But I do want to echo what you just said, that I
23 think that the interpretation -- that this very
24 interesting approach biological equivalents, but endorsing
25 them as being safe or at the hazard level is beyond the

1 scope of this Committee. And I feel like, although I
2 appreciate the work that's being done, I feel we should
3 stick to providing the most accurate exposure data that we
4 can, to endorse your comments.

5 ACTING CHAIRPERSON BRADMAN: So at this point, I
6 think then we're actually getting back on time here. We
7 now have a period for open public comment of up to 15
8 minutes.

9 MS. HOOVER: Actually, this is Sara Hoover of
10 OEHHA. Before we move off, so the open public comment
11 period is actually closing Dr. Sobus's item, and it's not
12 related to Dr. Sobus.

13 So before we close off, I wanted to just open it
14 to, you know, any staff -- Program staff or, you know,
15 important Program advisors to just think about or comment
16 on going forward are there ways that people envision, you
17 know, continuing? I mean, we have -- I find Dr. Sobus to
18 be really interesting in what he's doing, a great
19 opportunity for the Program to work with EPA. So more
20 comments about, you know, what are intersections between
21 the kinds of things he's doing and our Program? Any
22 thoughts at all in that regard before we move off into the
23 open public comment? So anybody at all in the Program or
24 on the Panel thinking in those terms?

25 ACTING CHAIRPERSON BRADMAN: Dr. Fenster.

1 DR. FENSTER: Hi. I really enjoyed the
2 presentation. And I found myself also feeling like a
3 field epidemiologist, in that work that say CHAMACOS has
4 done, literally collecting samples in the field where it's
5 difficult to even get samples back to a lab in terms of
6 assuring quality control, you know, makes me feel like the
7 work that EPA is doing is particularly of interest to find
8 ways where we can extrapolate from those more ideal data
9 collection methods to other ways we can collect data from
10 a very disparate population in California, because I think
11 that's really, to me, where the -- you know, the value in
12 the future and continued discussion, in terms of us being
13 able to extrapolate lessons from more of an ideal
14 collection with a particular group of people that you have
15 been able to use to collect data, in terms of the second
16 piece of your -- of your presentation. Because I think
17 that, you know, it's a very rare and it's very great data
18 collection methods. And if we can extrapolate and ways we
19 can be more efficient in collecting our data, that would
20 be a great collaboration.

21 DR. SOBUS: This is Jon Sobus again. I wanted to
22 make one other point that -- I know I covered a lot of
23 material very quickly, but one of the things I didn't have
24 a chance to get into is something that we talked about
25 earlier today and that's -- you know, we covered uses of

1 existing data, and collection of new samples.

2 What we're really thinking about now is doing
3 this kind of untargeted analysis. And at the Agency,
4 particularly in the Chemical Safety for Sustainability
5 Research Program, we have the charge of prioritizing very
6 large lists of chemicals based on anticipated exposure,
7 hazard, and ultimately risk.

8 So we've been developing models and different
9 testing techniques for trying to make predictions on a
10 very large number of chemicals. And ultimately to
11 evaluate that, we think biomarkers will be a terrific tool
12 and measurements in general. So we're really starting to
13 think about and apply some methods for doing some of these
14 untargeted type measurements.

15 So I'd like to put out there that -- so we don't
16 reinvent the wheel, that if groups are being formed here
17 in the State, we would love to be part of that discussion
18 to think about, you know, the different analytical
19 platforms that are being used, the different media that
20 are being measured, and to think about what EPA could
21 contribute, so that again we're not reinventing the wheel,
22 that we have a particular niche, and hopefully, it would
23 be a very nice relationship to start.

24 ACTING CHAIRPERSON BRADMAN: Dr. Quint.

25 PANEL MEMBER QUINT: Julia Quint.

1 Yeah, I really enjoyed reading your papers and
2 enjoyed the talk. And I think, for me, since joining the
3 Panel, what's most important here, what we're all trying
4 to get at is reduction of exposure. And, you know, risk
5 aside, we really want to reduce the hazards. So I think
6 the -- if there are ways to collaborate on how when
7 you're -- we're doing these studies to collect better
8 exposure information would be really, really helpful,
9 because often we can come up with levels in bodies, but
10 then trying to figure out where those chemicals came from
11 is the real challenge.

12 And so -- and I think your papers are the first
13 that I've seen that really sort of honed in on that whole
14 exposure relationship to bio -- I mean, I'm sure others
15 have -- but to put it so clearly. You know, there are
16 occupational studies where you have very good information
17 about exposures. And we've had biological exposure
18 indices in occupational health for a long time, but it's
19 gone nowhere in terms of reducing hazards, as far as I'm
20 concerned, because the standards are -- the PELs are
21 still -- you know, have a lot of risk attached to them.
22 So we've not used it in terms of chronic toxicity the way
23 we should have.

24 So anything that we can get at in terms of
25 collecting better exposure information, better

1 questionnaires, however we do that, would be tremendously
2 helpful to this Program. And collaborations on that level
3 would be wonderful.

4 ACTING CHAIRPERSON BRADMAN: I'll make one last
5 offer.

6 I'm sorry. Dr. Zeise.

7 DR. ZEISE: Just one more point with respect to
8 the collaboration. It would be absolutely wonderful to
9 work more with you, and -- Lauren Zeise with OEHHA.

10 And one of the big issues with the non-targeted
11 sampling that's been particularly difficult is figuring
12 out the metabolites and coming up with a reference list
13 for metabolites, and I think making some progress in that
14 area. I don't know what you all are doing in that regard,
15 but we're finding it particularly difficult. So I don't
16 know if you want to comment on that.

17 DR. SOBUS: Just to respond to it. Jon Sobus.
18 To the best of my knowledge, it's something we've been
19 talking about too. I don't believe we've made any
20 headway. I would say we're fairly new to the field of
21 trying to get into untargeted work, but that whole
22 metabolism issue is something that has come up, and
23 there's been discussions at the high management level
24 about it.

25 So it's something that we're taking into

1 consideration as we plan for how we're going to do this
2 work, and as we try and align instrumentation, and again
3 think about chemicals and samples to look at, and figure
4 out just the best strategies going forward. So again, you
5 know, I think we're probably having a lot of the same
6 discussions internally, but I think it will be very
7 fruitful to have those discussions in a larger group.

8 ACTING CHAIRPERSON BRADMAN: Just one last
9 comment or perhaps an opportunity for collaboration. We
10 have a set of samples collected from three to six year
11 olds spot and 24-hour samples collected over a week
12 period. And we've been wanting to conduct or complete a
13 collaboration with this Biomonitoring Program to look at
14 phenols and phthalates and other metabolites in those
15 samples to get at issues around, within, and between
16 variability.

17 We published one paper on pesticide metabolites,
18 but there's a lot more that can be done with that. And
19 that's perhaps something that we could move forward on
20 perhaps try to get resources to measure them and to do the
21 whole set. So there might be an opportunity here to
22 perhaps address some of the questions that you're
23 interested in and also the Program here.

24 So again, we're right on time actually now at
25 4:20 to close the previous discussion around the

1 presentation. And we now have a open public comment
2 period. And then after that, we'll have a wrap-up and
3 adjournment. It looks like we do have a public comment
4 from Nancy Buermeyer.

5 MS. BUERMEYER: Buermeyer.

6 ACTING CHAIRPERSON BRADMAN: Buermeyer -- thank
7 you -- from the Breast Cancer Fund.

8 MS. BUERMEYER: Thank you very much. And I know
9 we're -- it's late in the day, so I'll try to be brief.
10 And I just wanted to take a minute to thank the Panel for
11 all the work that you do to support this Program and
12 clearly the homework you do before you get here, and your
13 comments here. And to thank the staff of the
14 Biomonitoring Program, which I know works tirelessly day
15 and night putting all these materials together, and
16 creating a world-class Program that we in California are
17 extremely, extremely proud of.

18 We've geeked out a little bit today talking about
19 metal speciation and validated methodologies and
20 intraclass correlation coefficients, which as an advocate
21 I have no idea what that is --

22 (Laughter.)

23 MS. BUERMEYER: -- but you sounded really smart
24 explaining it, Dr. Sobus, so thank you.

25 (Laughter.)

1 MS. BUERMEYER: And I just wanted to sort of take
2 a step back to let you know that this Program is really
3 valuable -- is really valuable to folks outside this room.

4 The Breast Cancer Fund organized a letter to the
5 Governor asking for State funding for this Program, given
6 the challenges you'll have with the loss of at least some
7 of the CDC funds.

8 So we organized a sign-on letter to the Governor.
9 And I just wanted to take one minute to read you the list
10 of organizations that signed this letter and support this
11 Program really strongly:

12 The Breast Cancer Fund, surprisingly, California
13 Healthy Nail Collaborative, California National
14 Organization for Women, Center for Environmental Health,
15 Clean Water Action, Coalition for Clean Air -- and please
16 excuse my Spanish on this -- Komite civico del Valle,
17 Commonweal Biomonitoring Research Center -- Davis in
18 absentia -- the Environmental Working Group, Friends of
19 the Earth, Natural Resources Defense Council, Pesticide
20 Action Network, Physicians for Social Responsibility Los
21 Angeles, San Francisco Bay Area Physicians for Social
22 Responsibility, and the United Fire Service Women, which
23 is an organization of women firefighters in San Francisco.

24 And I'm sure there are lots more organizations
25 that are out there that would have signed this had they

1 had time and I had time to track them down. But I just
2 want you to know that what you do is really appreciated
3 out in the world by the communities that are impacted by
4 these chemical exposures, and to say thank you from all of
5 them for the work that you do and for the work that the
6 Panel does in supporting this Program.

7 Thank you.

8 ACTING CHAIRPERSON BRADMAN: Well, I think then
9 we are approaching the end of today's meeting and now,
10 time for a wrap-up and adjournment.

11 I want to announce that a transcript of this
12 meeting will be posted on the Biomonitoring California
13 website when available.

14 Also, a reminder that the next meeting of our
15 group will be on July 10th also in Oakland, and also to
16 let you know that the conference facility here will close
17 promptly at 5:00 and that we recommend heading down to the
18 lobby as soon as we're done.

19 (Laughter.)

20 ACTING CHAIRPERSON BRADMAN: So if you need to
21 schmooze, we'll have a little time up here, but you should
22 schmooze down in the lobby downstairs.

23 And I think Dr. Alexeeff, do you -- are you going
24 to provide a wrap up for today's meeting?

25 DIRECTOR ALEXEEFF: No. I was just going to say

1 we would be -- we will be posting the transcript on the
2 website when that's done. And we did discuss designating
3 and prioritizing chemicals today, and that's a lot of the
4 hard work of the Panel. We had a great presentation from
5 Dr. Sobus, and also updates of the laboratory and the
6 other staff work that's going on.

7 I want to thank the Panel for again taking time
8 out of their busy schedule to come here to advise the
9 State on this very important Program and giving us
10 direction, and utilizing the resources that we have in
11 this Program wisely, in helping us to collaborate with
12 other agencies, universities, and departments in the
13 State.

14 So thank you very much.

15 ACTING CHAIRPERSON BRADMAN: I think we're
16 officially done.

17 Thank you.

18 (Thereupon the California Environmental
19 Contaminant Biomonitoring Program, Scientific
20 Guidance Panel meeting adjourned at 4:24 p.m.)
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C E R T I F I C A T E O F R E P O R T E R

I, JAMES F. PETERS, a Certified Shorthand Reporter of the State of California, and Registered Professional Reporter, do hereby certify:

That I am a disinterested person herein; that the foregoing California Environmental Contamination Biomonitoring Program Scientific Guidance Panel meeting was reported in shorthand by me, James F. Peters, a Certified Shorthand Reporter of the State of California, and thereafter transcribed under my direction, by computer-assisted transcription.

I further certify that I am not of counsel or attorney for any of the parties to said meeting nor in any way interested in the outcome of said meeting.

IN WITNESS WHEREOF, I have hereunto set my hand this 10th day of April, 2014.



JAMES F. PETERS, CSR, RPR
Certified Shorthand Reporter
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