MEETING

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ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

ENVIRONMENTAL CONTAMINANT BIOMONITORING PROGRAM

SCIENTIFIC GUIDANCE PANEL

CAL/EPA BUILDING

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A P P E A R A N C E S

PANEL MEMBERS:

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

Scott Bartell, M.S., Ph.D.

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

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

Thomas McKone, Ph.D.

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

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT:

Dr. Lauren Zeise, Acting Director

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

Ms. Frank Kammerer, Staff Attorney

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

DEPARTMENT OF PUBLIC HEALTH:

Dr. Michael J. DiBartolomeis, Chief, Exposure Assessment Section, Environmental Health Investigations Branch, Lead of Biomonitoring California

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

DEPARTMENT OF TOXIC SUBSTANCES CONTROL:

Dr. Myrto Petreas, Chief, Environmental Chemistry Branch

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

GUEST SPEAKERS:

Vanessa Galaviz, Ph.D., M.P.H., Associate Public Health Scientist, Office of the Secretary, California Environmental Protection Agency

Chris Simpson, Ph.D., Professor, University of Washington

ALSO PRESENT:

Ms. Nancy Buermeyer, Breast Cancer Fund

Mr. Tom Jacob, Chemical Industry Council of California

Dr. Veena Singla, Natural Resources Defense Council

I N D E X

	PAGE
Welcome	
Lauren Zeise, Ph.D., Acting Director, Office of Environmental Health Hazard Assessment (OEHHA)	2
Overview of the Meeting	
Asa Bradman, Ph.D., Chair, Scientific Guidance Panel (SGP)	3
Introduction to Morning Session, Dr. Bradman, SGP Chair	5
New Results for 1-Nitropyrene Metabolites in Children and Underground Miners	
Presentation: Chris Simpson, Ph.D., Professor, University of Washington	7
Panel Questions	21
Urinary Metabolites of 1-Nitropyrene in US-Mexico Border Residents	
Presentation: Vanessa Galaviz, Ph.D., M.P.H., Associate Public Health Scientist, Office of the Secretary, California Environmental Protection Agency	32
Panel Questions	40
Repeated Measurements of PAH Metabolites in Women–Initial results from a sub-study for Women's Health and the Environment (WHE)	
Presentation: Ulrike Luderer, M.D., Ph.D., Professor, Center for Occupational and Environmental Health, School of Medicine, University of California, Irvine	47
Panel Questions	59
Morning Session Discussion	
Panel and Guest Speaker Discussion	68
Public Comment	86
Wrap up	91
Afternoon Session	104

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

	PAGE
Laboratory Updates	
Presentation: Jianwen She, Ph.D., California Department of Public Health (CDPH)	104
Panel Questions	115
Presentation: Myrto Petreas, Ph.D., M.P.H., Department of Toxic Substances Control (DTSC)	120
Panel Questions	133
Public Comment	136
Panel Discussion	138
Program Update	
Presentation: Michael DiBartolomeis, Ph.D., D.A.B.T., CDPH	142
Panel Questions	161
Public Comment	168
Panel Discussion	170
Open Public Comment Period	185
Wrap-up and Adjournment	186
Reporter's Certificate	188

P R O C E E D I N G S

DR. PLUMMER: All right, everyone. Let's go ahead and gather for the meeting. Take your seats.

So I just want to make a few announcements. So today's meeting is available via webcast. And so we ask you to please speak directly into the microphone and introduce yourself before speaking today. And this is for the benefit of the people participating via the webcast and also for our transcriber.

So the materials for today's meeting were provided to SGP members, and they were also posted on the Biomonitoring California website. And a small number of copies of the agenda and the presentations are available at the table near the entrance of the auditorium. A sample SGP packet, which includes background references for the morning session is also available for viewing at this table.

Today we will take one break at 1:00 p.m. for lunch for about an hour and a half, returning around 2:30, 2:25. The restrooms are located out the back doors and to the left as you exit. And the emergency exits are located to my left there, to my right there, and also out the back as well.

And with that, I'd like to introduce Dr. Lauren Zeise, Acting Director of the Office of Environmental

Health Hazard Assessment. Lauren.

ACTING DIRECTOR ZEISE: Good morning. Good morning, everyone. I'd like to welcome everyone in the audience and on the web to this meeting of the Scientific Guidance Panel for the California Environmental Contaminant Biomonitoring Program, which we also call Biomonitoring California. And I want to thank you all ahead of time for your participation in this meeting.

I just want to take a minute or two to send good wishes to Meg Schwarzman who is recovering from a very bad bicycle accident. She's a member of this Panel. And I'd like to let everyone known she's home. She came home on Tuesday. And at the back of the table, we have a recent picture of Meg celebrating her first -- her son's very first birthday in the hospital, as well as the newspaper article that discusses the accident. So please feel free to take a look at the materials at the back of the room.

Meg has really made amazing progress and she wants every -- she sends everyone her good wishes and she wants everyone to know she'll be back. So it will be a long recovery, but we're going to see Meg again fairly soon, I think.

So at the last SGP meeting it was held in Richmond on November 18th, 2015. And at that meeting, we heard from representatives of the CDC and State

biomonitoring programs across the U.S., and discussed issues of common interests, provided input on best practices for returning biomonitoring results to study participants during a special session on this topic. And this included presentations by Dr. Rachel Morello-Frosch of UC Berkeley, and Duyen Kauffman at CDPH, and an in-depth discussion with the guest speakers and audience.

So the Panel unanimously recommended at that meeting that two chemicals classes ortho-phthalates and perfluoroalkyl and polyfluoroalkyl substances be added to the list of priority chemicals for Biomonitoring California. So more information on the November meeting is available on the biomonitoring website at www.biomonitoring.ca.gov.

And now, I'll turn the meeting over to the Chair of the SGP, Dr. Asa Bradman.

CHAIRPERSON BRADMAN: Thank you. And thank you everyone for attending today. You'll have to excuse my voice is a little bit rough today. Getting over a cold here, but I don't think I'm contagious.

So we're going to review a few things before we get started. And I want to go over the goals of today's meeting. We have a few different components today. I think it will be a very interesting discussion this morning, which will involve participating in a special

session on exposure to diesel exhaust, and other sources of polycyclic aromatic hydrocarbons, and also to provide input to the Program on next steps related to this new information and where we want to go forward in addressing diesel as a potential target for biomonitoring. We're going to also hear laboratory and Program updates and provide input. That will be most of our afternoon agenda.

And then just a reminder from past meetings for each agenda topic, we're going to have time for Panel questions and discussion. There will also be opportunities for public comment and then also additional public -- Panel discussion and input. And just a reminder about public comments, if you'd like to make a comment on an agenda item, please fill out a comment card, which can be obtained from the table near entrance of the auditorium. Turn the cards into the Laurel Plummer. Laurel, if you could raise your hand. Thank you.

And for those of you who are listening to us through the web, you can provide comments via email at biomonitoring@oehha.ca.gov. OEHHA being O-E-H-H-A. So biomonitoring@oehha.ca.gov. Emailed comments relative to the topic under discussion will be read aloud during the meeting.

As usual, public comments will be subject to time limits. And if needed, the time allotted will be divided

equally among all the individuals wishing to speak on that agenda item.

Please keep comments focused on the agenda topics being presented and there will be an open public comment period as the last item of the day. So on -- at that point, you can make comments or submit questions about anything relevant to the Biomonitoring Program.

So I want to now introduce the morning session. At the November -- those of you who were there, you may recall at the November 2014 meeting, the Scientific Guidance Panel encouraged the Program to pursue method development to measure 1-nitropyrene metabolites as nonspecific urinary biomarkers for diesel exhaust exposure. The Panel also discussed complementary strategies to evaluate diesel exhaust exposures and potential health impacts, including ambient air monitoring, exposure modeling, the measurement of nonspecific markers of inflammation, and genotoxicity.

So they've come to follow up on this. I think we're going to have a really interesting discussion this morning -- for this morning's session, which will review recent biomonitoring findings on 1-nitropyrene metabolites and other PAH metabolites in various populations, some in California and some elsewhere.

The primary goal of the session is to discuss

strategies for studying communities that maybe highly exposed to diesel exhaust and/or other sources of PAHs in California, as well as approaches for using biomonitoring to evaluate public health impacts of California's regulations aimed at reducing emissions from diesel sources.

And I think that will be a particularly interesting topic for discussion today about whether we can really conduct studies that can look for changes related to changes in emissions.

As a reminder, when we talk about community in terms of Biomonitoring California, a community can be geographically or non-geographically based, i.e. it can include a location like, for example, those living near a port or an occupational population. We'll first hear presentations from three experts in the field, with time for questions after each presentation.

Then the Panel will have an in-depth discussion on these topics with our guest speakers and the audience. So again, we look forward to everyone's input on these discussions.

So first, I want to introduce Dr. Chris Simpson, who spoke with us a number of months ago. Dr. Simpson is a professor in the Department of Environmental and Occupational Health Sciences in the School of Public

Health at the University of Washington, where he directs the Exposure Sciences Program. His research involves applying state of the art analytical chemistry techniques to understand and control human exposures to hazardous chemicals. He has a particular interest in biological monitoring of chemical exposures in both occupational and non-occupational settings. And for the past 10 years his group has been pursuing research towards development of a potential biomarker of exposure to disease exhaust.

Dr. Simpson will present new biomonitoring results for 1-nitropyrene metabolites in children and underground miners. So with that introduction, we look forward to your presentation. Thank you.

(Thereupon an overhead presentation was presented as follows.)

DR. SIMPSON: Thank you very much for that introduction and the invitation and opportunity to talk to you about nitropyrene again today. About a year or so ago, I introduce this as a potential marker for diesel exhaust.

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DR. SIMPSON: And so I'll begin with just a quick recap. So 1-nitropyrene is formed by nitration of polycyclic aromatic hydrocarbons within diesel engines. It's a relatively specific particle-associated marker for

diesel exhaust. That said, it's not -- it's important to note that it's not absolutely unique to diesel exhaust. So in the IARC monograph, you'll find several examples where 1-nitropyrene is generated by non-diesel sources.

More recently, some studies out of China have reported that 1-nitropyrene emissions are derived also from residential combustion of low grade coal. That said, it is the case that generally 1-nitropyrene emissions that people are exposed to, especially here in the U.S., are derived predominantly from diesel exhaust.

It's also worth noting that unlike the other nitropyrene isomers, 1-nitropyrene is not formed to a significant extent by photochemical reactions. Again, there's been some recent data that showed that it is possible to form 1-nitropyrene photochemically under some discussions. But again, this is expected to be a very small contribution to the total 1-nitropyrene ambient concentrations.

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DR. SIMPSON: I want to acknowledge that emission controls on modern diesel engines have come along way, and have dramatically reduced 1-nitropyrene emissions from the engines themselves. That said, 1-nitropyrene is still emitted by the contemporary diesel fleet. And as an example of that, the attached graphic here is based on

measurements that we made in Seattle in 2012. That map that you're seeing is the industrial area of the Duwamish in south Seattle.

We collected two-week integrated air particulate samples at 20 locations within the study area, and then developed a land-use regression model that modeled the spatial distribution of the 1-nitropyrene. And that's the colored heat map that you can see.

Diesel source specific variables, including proximity to railroads, the density of truck traffic, and on-road measurements of mobile black carbon were all significant components in this land-use regression model. And so this indicates that variables associated with diesel truck traffic and diesel railroad traffic are -- they're important predictors of the spatial variation of 1-nitropyrene concentrations at least in 2012 in the Seattle area.

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DR. SIMPSON: So this slide shows the metabolic pathways of 1-nitropyrene in mammals. In vivo studies in rats suggested that hydroxylated and the n-acetylated metabolites, the two compounds highlighted in yellow at the second level of the slide, are the most abundant compounds in mammalian urine. And certainly, they're the compounds that we have found to be the most abundant in

the human urine samples that we've measured in my lab.

I'll also note that the assay that we used is not able to detect 1-aminopyrene, which is one of the other metabolites shown on the slide here. There are data from some other researchers, from both human and animal studies, that indicate that 1-aminopyrene is formed following exposures to 1-nitropyrene. And so this too may be a potentially useful biomarker of exposure to diesel exhaust.

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DR. SIMPSON: So this chart summarizes measurements of 1-nitropyrene and levels of the specific urinary metabolite 8-hydroxy 1-nitropyrene from various studies that have been undertaken in our laboratory at the University of Washington. And what the plot is showing is that higher metabolite levels on the Y axis are associated with higher levels of measured exposure to 1-nitropyrene shown along the X axis.

However, in the two occupational studies, that we undertook, we found that at the level of the individual, the urinary biomarker levels were not significantly associated with the measured personal exposure on the day of urine collection. So we see there's a dose response at the group level, but not at the individual level.

And that prompted us to think about the temporal

relationship between exposure and biomarker level. So we undertook a study in a cohort of underground miners in which we were able to collect serial urine samples from the -- from diesel exposed workers, and that will allow us to explore more fully the time course of 1-nitropyrene metabolite excretion following the inhalation exposure to 1-nitropyrene. So that study I will describe in the next several slides.

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DR. SIMPSON: So the study took place in a large underground metal mine in the U.S. It had a worker population of about 1,300 workers where they use extensive use of diesel engines, and being underground there's a limited amount of ventilation that's possible, and so the workers are potentially exposed to relatively high levels of diesel exhaust.

We enrolled 20 subjects in the study, and we ensured the subjects had job titles that had them either at the surface operations -- actually, at the face of the mine where the active mining was taking place or in underground maintenance shops. And previous work with miners and diesel -- looking at diesel exposure has indicated that exposure is highly correlated with the kind of task that the workers are doing, and especially their location within the mine. And so ensuring that we had

subjects at the surface, at the mine face, and then these underground shops helped to ensure that we had a range of exposures amongst the workers.

We undertook four sampling campaigns, each campaign lasted for four days. This particular mine all of the workers worked four days on and four days off. And those are long work shifts, at least 10 hours in the mine with another couple of hours getting down into the mine and then getting back up to the surface.

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DR. SIMPSON: So on those workers, we measured personal exposure by measuring 1-nitropyrene and elemental carbon using small personal sampling pumps and filters. We did not have sufficient equipment to monitor full shift exposures on all workers on every day. And so on each of these sampling campaigns, we collected the personal exposure samples for subjects 1 to 10 on days 1 and 3 of their work week. And for subjects 11 to 20, it was on days two and four of the work week.

For the urine samples, we were able to collect pre-shift and post-shift samples for all workers every day. So we have the full range of urine measurements, even on days where we had not collected personal exposure measurements. We also had subjects complete a daily questionnaire regarding where they were working in the

mine and the specific tasks that they were doing, so that we could use that questionnaire to predict exposures on days that we had not measured the personal exposure.

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DR. SIMPSON: So this current slide indicates the variability in exposures amongst the workers. So just to orientate you to it, the numbers 1 to 20 along the bottom of the slide represent the 20 different workers. The nitropyrene concentration is shown on the Y axis, and that's a log scale or a log base 2 scale. And the -- each of those bars represents the distribution of the measurements for each worker. We've also colored those bars representing either the surface, the underground work shops or the face locations. And you can see that, in general, the face locations in blue have higher levels of exposure than the surface locations, and orange have lower levels of exposure. That's also summarized in the table at the bottom of the slide.

The geologists, we separated those out as a separate category. Some days they were working at the surface and some days, they were working down at -- marking at the face to indicate where mining activities would take place. And so there, they suffered a much wider range of exposures because they were working in different parts of the mine.

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DR. SIMPSON: This slide is a similar layout, but now we're looking at the metabolite levels, and specifically the 8-hydroxy nitropyrene metabolite level. And again box plots showing the distribution of data for each of the 20 workers. And in this case, we do not see the same obvious stratification of exposure based on job location that we had seen in the personal air measurements. And the reason for that, I think, can be explained in the following slide.

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DR. SIMPSON: And so in this case, we're looking specifically at the urine measurements. We're not considering exposure at all. And we're looking at variation in those urine biomarker concentrations across the course of the workweek. So remember again, these folks work four days on and four days off. The pre-shift urine sample on day one, one would expect would be the -- would have the lowest concentration of biomarker level. And indeed, that's what we see, both for the 6-hydroxy compound and for the 8-hydroxy compound.

But then we see that as we progress across the week measuring those post-shift urine samples, the concentration -- or the biomarker concentration continues to step up across the week. And it really has not

stabilized by the end of the week. And so that's indicating that the metabolite levels are building up in the workers. They're continuing to accumulate in the workers as the exposure -- as they're exposed day after day across the week.

I should note that we also looked at the day-by-day exposures, and there was not a trend of an increasing air exposure across the week. In fact, if anything, the exposures tailed off towards the end of the week as perhaps the mining operations were slowing down a little bit at the end of each week.

So in the context of -- well, one way of interpreting this data, so in a setting where workers or community members are being exposed repeatedly, so day by day, to nitropyrene, the biomarker level is going to average out exposures over the preceding several days, and so it's going to average out, to some extent, the day-to-day variation and ambient exposures when you have a setting of repeat exposures as you would in a community setting.

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DR. SIMPSON: Oh, I should qualify, that that specific set of data I'm showing with these metabolite levels that was for the first group. And so that was the group of workers that, in general, had the highest

exposures to 1-nitropyrene. We saw a similar trend for the shop group, although not quite as clear, because their exposures were somewhat lower, and we really didn't see any across-week trend in the exposures for the surface group. Their exposures were essentially the same as what one would expect for people that are simply exposed to ambient concentrations.

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DR. SIMPSON: The final slide that I'll show on this diesel miner study is that the plots on the right represent a prediction model where predicting -- where we're regressing the measured urinary metabolite concentrations measured versus predicted, where our prediction model includes in the work location, the day of the week and additional exposure-related variables, such as the self-reported time that the workers said they were exposed to diesel exhaust, and whether or not they were using a respirator when they were -- when they felt they were exposed to diesel exhaust or not.

And so what the takeaway from this specific slide is that worker-specific measures of diesel exposure are highly correlated with the biomarker levels. The more activities the workers were doing that resulted in diesel exposure, the higher level of biomarker that was observed in the urine.

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DR. SIMPSON: Okay. So the second study that I want to present data on is a pilot study that took place here in California examining community exposures to diesel exhaust. So this was a study that took advantage of some urine samples that had previously been collected by Dr. Bradman, the study -- the urine samples were obtained from children, primarily Mexican or Mexican-American, primarily low income, and near Salinas shown in the map on the bottom of the slide and Oakland, shown in the map on the top of the slide.

The original study was designed to look in part at pesticide exposures and the effect of an organic diet on pesticide exposures. However, given where the subjects lived for this particular study, we were able to categorize the subjects as either highly traffic exposed or low traffic exposed based on where they lived. So those that were lived -- that lived in Oakland, near the I-880 freeway were categorized as having high -- presumptive high exposure to diesel exhaust and to traffic emissions. And conversely, those living in Salinas had -- were categorized as having presumptive low exposure to vehicle exhaust.

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DR. SIMPSON: When we look at the biomarker

levels that we measured in this pilot study shown on the left for the raw urine concentration and for the right as creatinine corrected urinary concentration, we see that for both of the metabolites, urine urinary levels were two- to three-fold higher. And the samples from Oakland, the presumptively high exposed group, compared to the children from Salinas, which was the presumptively the low exposed group.

These differences, while not -- are not statistically significant, but remember this is a pilot study with only 10 samples from the high exposed and the low exposed group. And certainly, the trend here is exactly what we would expect based on the presumptive exposure.

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DR. SIMPSON: Similarly, we were able to try and drill down a little bit into the individual exposure prediction. And so we examined the correlation between the urinary biomarker levels and the subject's traffic exposure, as measured by or as predicted by the traffic density within various circular buffers surrounding the homes where the subjects lived.

So that's a 500 meter, 1,000 meter, or 2,000 meter buffer. And what we see, shown in the table at the bottom there, is that the -- in general, the exposure was

positively correlated with the traffic density, particularly in those 1,000 meter and 2,000 meter buffers for the two specific urinary metabolites. Again, the correlations were not statistically significant, but they were moderate and they were in the direction that we would have predicted based on the higher exposures being associated with higher levels of urinary biomarker.

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DR. SIMPSON: Okay. So just a couple of summary or concluding comments. So we now have shown in approximately six or so different studies that these 1-nitropyrene metabolites can be reliably detected in human urine, including from individuals with ambient concentrations -- exposed to ambient levels of diesel exhaust. So we can see these in highly exposed subjects, but we can also see them in subjects with community exposures to diesel exhaust.

All of these data strongly suggest that those urinary metabolite levels increase as exposure to diesel exhaust increases, both with the personal exposure measures and also with the predicted exposures using regression models.

We should note, by way of qualification, that we don't yet know the extent to which exposures, other than diesel exhaust, contribute to urinary 1-nitropyrene

metabolite levels. That's perhaps an area of -- that needs to be considered further. But certainly the data that we've shown so far indicates that the urinary levels are associated with the inhalation exposures.

From a quantitative sense, we don't have a very clear idea of how strong the relationship is between inhaled nitropyrene and urinary metabolite levels. And in large part, that is because we have not yet fully completed the pharmacokinetic evaluation to determine what is the appropriate window of exposure to associate with a specific spot urine sample.

In summary, I believe that these metabolites continue to show promise as biomarkers of exposure to diesel exhaust. I have identified some important knowledge gaps that we still need to answer before we can complete the quantitative evaluation or association between the inhalation exposure to these compounds, specifically related to diesel exhaust, and the biomarker levels. But in the various studies, I have shown, they all point to -- you know, to a robust association between diesel exhaust exposure and the biomarker levels.

Thank you.

CHAIRPERSON BRADMAN: Thank you, Dr. Simpson, for that presentation. It's really fascinating. I think it points to a lot of opportunities for discussion and follow

up.

So we have a -- right now, we have about 10 minutes for Panel questions. We're running a little bit early so far, so that's good.

So, Dr. Luderer.

PANEL MEMBER LUDERER: Thank you. It was a really interesting presentation. One of the things I wanted to ask you about was the concentrations of the nitropyrene metabolites in the miners versus the children. Am I seeing that correctly, that they seem to be higher in the children, the picograms per gram of creatinine -- or milligram of creatinine?

DR. SIMPSON: So this -- let's see, this is a linear scale for the children. Going back to the -- you're right, that is also linear. So that is an interesting observation. We were surprised that the biomarker levels in the miners were not higher. In fact, the biomarker levels, in general, were kind of on the lower end of what we've seen in other populations.

Of note, this population of miners is in a rural part of Montana. And so their ambient exposures to traffic related pollution and diesel exhaust are much lower than what we would expect for an urban population. And so that is the -- that is the best explanation I have for the fact that these urine levels -- the absolute

levels amongst the miners were lower than what we saw in the California samples.

PANEL MEMBER LUDERER: Just a follow up real quick. Yeah, that's very interesting, because I think it highlights the importance of ambient exposures that -- just in urban areas within the State of California. The other question I had was how did the air -- the air levels in the mine compare to say in the air levels that have been measured in Oakland? You know, do you know, have any --

DR. SIMPSON: So we did not measure nitropyrene in the air in Oakland. I'm not -- so for the nitropyrene, I'm not aware that there is existing data on that. Almost certainly there's black carbon data for Oakland, and so we could look at that and compare that to the elemental carbon levels in the mine.

I should note that the elemental carbon levels in the mine were, in fact, well below the occupational standard. So the emission control technologies and the ventilation that they're using in that particular mine are very effective. One could surmise that the only reason they let us into that mine was they knew we would not find a violation.

(Laughter.)

CHAIRPERSON BRADMAN: I'm just curious where the

mine was located?

DR. SIMPSON: So it's in Montana. I'm not at liberty to tell you where in Montana, because the mining industry is somewhat sensitive to potential liability and so on and presenting data on worker exposures. So I can tell you that it's a large platinum mine, but I'm not at liberty to say which specific mine it is.

CHAIRPERSON BRADMAN: Were there any -- you mentioned that the black carbon levels were low. Were there any other measures of ventilation, like carbon monoxide or other -- CO2 or --

DR. SIMPSON: So we -- on the workers, we were only measuring particle related measures. We did have some area measurements of CO2, CO, and NO2. The CO was well below -- well, the CO was well below the regulatory standard. The NO2 occasionally was a problem. So the way the mines have been able to get their particle emissions under control is by using oxidation catalysts, and that has increased the NO2 emissions. So in order to get in compliance with the particle regulations, they now have a concern in times of violating the NO2 regulation.

CHAIRPERSON BRADMAN: Dr. Quintana.

PANEL MEMBER QUINTANA: Hi. Thank you for that presentation. Do you think an additional reason that the children may have had quite high urinary metabolites might

be due to the fact that with their small body size and increased breathing rate, that even with a lower exposure, they could potentially have a very high internal dose or perhaps even have metabolic differences that might lead to observed differences?

DR. SIMPSON: That's a very good question. So there -- there have been no -- in fact, this California data is the first data that I'm aware of that has reported nitropyrene metabolite levels in infants. And so there's been no studies to look at the potential metabolic differences between adults and children. But you're absolutely right, one of the reasons why children are considered an at-risk group is that their dose per mass of body weight is higher than it is for an adult, because they -- because of the higher relative ventilation rate that they have.

CHAIRPERSON BRADMAN: Dr. McKone.

PANEL MEMBER McKONE: I want to move to a different question in terms of chemical properties. And this is not very volatile, right?

DR. SIMPSON: Exactly, it's --

PANEL MEMBER McKONE: So your understanding is most of this is -- most of what would be going into an individual is bound to the particle phase as opposed to being a mix of particle and gas, like some -- some of the

nitro-PAHs have enough volatility that you have to keep track of two phases --

DR. SIMPSON: Exactly.

PANEL MEMBER McKONE: -- if you really don't want to --

DR. SIMPSON: Yeah. So you're absolutely right. The literature on 1-nitropyrene demonstrates that as present, we say exclusively in the particle phase by which we mean greater than 95 percent, even greater than 99 percent under typical environmental temperatures.

CHAIRPERSON BRADMAN: A follow-up question related to Tom McKone's. Do we have a sense about how much of the exposure could be non-dietary ingestion, if it's in, you know, particles, so there may be some house dust or larger particles, maybe not fully inhaled and then -- so do we have a sense of how the 1-nitropyrene may --

DR. SIMPSON: So we do not have a quantitative sense of that. And the IARC monograph that lists prior measurements of nitropyrene by environmental media, there are certainly examples where nitropyrene has been measured in foodstuffs. Those studies have not -- are certainly not comprehensive in nature, and so they indicate that the potential for exposure via that pathway exists, but no studies to this point have looked to do a mass balance or

compare the relative importance of the inhalation pathway versus the dietary pathway for nitropyrene.

PANEL MEMBER BARTELL: I just enjoyed your presentation. Thank you. But I had a quick question about the pharmacokinetics, which is the note you ended on. And I think you've hinted that, and certainly slide 10 suggests that, you know, there might be a relatively short half-life for some of the process involved in producing these metabolites, since you see these kind of rapid changes post-shift. I was just curious how you plan on proceeding with pharmacokinetic modeling? Are there animal data or any plans or is anybody working on sort of an animal pharmacokinetic model, or are you going to try to rely kind of solely on the observational data you have here to try to suss out the pharmacokinetics?

DR. SIMPSON: So from the point of view from my expertise, I'm not an animal toxicologist, and so I'll be relying on trying to fit models to our human data to extract the pharmacokinetic parameters that way.

There does exist in the literature a PBPK model for inhalation exposure to 1-nitropyrene that was developed I believe on rats. And so we can look at trying to use that -- try that -- apply that model with the human data to see if that model fits the data reasonably.

The only other studies that I'm familiar with

with rats and so on have been -- have essentially been single dose studies. And in the case of diesel exhaust, clearly we're typically interested in chronic exposure. And there's some challenges in translating results from a single exposure study to a chronic exposure situation.

PANEL MEMBER BARTELL: Thank you.

CHAIRPERSON BRADMAN: Dr. Quintana.

PANEL MEMBER QUINTANA: So have you thought of collaborating with some of the human controlled exposure to diesel exhaust studies, either yourself or I know there's archived samples from some of those known exposures, which tend to be a little high in level, but it might be interesting for pharmacokinetics.

DR. SIMPSON: Exactly. So we've started to do some of that work with colleagues at the University of Washington where they have a human exposure facility. We don't yet have the data from those particular studies.

One of my -- one thing that gives me pause, in terms of maybe lowers my expectations for that particular study is that as one might imagine, we really can't expose humans to very high levels for long periods in those controlled studies. And so you'd have the exposure protocol as a two-hour exposure to, I think, it's a 100 micrograms per cubic meter of elemental carbon, which is relatively high in terms of ambient exposure levels. But

once you compare that exposure to weaker ambient levels, then the controlled part of the exposure is actually not such a substantial piece of the integrated exposure over four or five days when you can't include in the ambient piece of it. So that's -- that may not be as much of a slam dunk as we might hope it would be.

CHAIRPERSON BRADMAN: Are there --

PANEL MEMBER LUDERER: I do have one more question.

CHAIRPERSON BRADMAN: Dr. Luderer.

PANEL MEMBER LUDERER: I just had a quick follow up to that. In that study, was there any kind of effort done sort of to have a wash-out before the exposure, you know, have participants spend time in a, you know, place where the air is known to be clean, you know, filtered?

DR. SIMPSON: No. So that particular study was really focusing on acute -- attempts to identify acute health outcomes associated with acute exposures. And so there was a cross-over design where they exposed people for two hours to diesel exhaust, and then a week or so later, they exposed people for two hours to filtered air, but they did not attempt to have a sustained period of low or zero exposure to diesel exhaust before the controlled exposure part of it.

CHAIRPERSON BRADMAN: I also have another -- I

have another follow-up question to the pharmacokinetics, the comments earlier. Do we have any sense of how the pharmacokinetics may differ say between children and adults. So if we look at the metabolites in children versus the adults, it's a possibility that the relative proportion of different pathways may result in a different balance of metabolites by age? And then related to that, is it also possible that there may be genetic or other factors that may change the balance of how the one 1-nitropyrene is metabolized, which might result in different relative proportions of the metabolites based on, well, either age or kind of within subject variability?

DR. SIMPSON: Sure. So the -- in terms of there being different proportions of metabolites for infants versus adults, I really don't have the expertise, in terms of developmental toxicology science to have a good sense of whether we would really expect there to be a different balance of metabolites.

We do have an idea of which enzymes are involved. And so there's clearly a group of P450s involved in the hydroxylation step. And, in fact, there's been some studies with human microsomes that kind of focus down on to which specific isoforms seem to be most important.

And clearly, those are polymorphic in humans, and

so there's the opportunity for there to be differences between people based on their -- the specific gene forms that they have.

Similarly, the acetylated metabolites, those are formed via the acetyltransferase enzymes. And those certainly are polymorphic in humans. We have fast acetylators and slow acetylators. And so we would expect that -- or we would hypothesize that that could lead to a different balance, and possibly a different time course, in terms of the excretion of these metabolites based on the specific genetic make-up that you have.

With some of the samples that we collected over from prior studies, where we were interested in exposure, we did go back and have done some genotyping for -- certainly for the N-acetyltransferases, so that we can try and look at that particular question. We don't have the data from those studies available yet though.

CHAIRPERSON BRADMAN: Are there any more questions from Panel members, discussion?

Okay. Well, I think at this point then we'll conclude this presentation. Thank you so much for contributing --

DR. SIMPSON: Thank you very much.

CHAIRPERSON BRADMAN: -- and look forward to additional discussion on this.

At this point then, I want to introduce Dr. Vanessa Galaviz. Thank you.

Dr. Galaviz has 10 years of experience in multiple aspects of environmental health, including industrial hygiene exposure -- industrial hygiene exposure assessment, genetic and molecular susceptibility to environmental pollutants, evaluating cumulative impacts, community-based participatory research, environmental justice, and air pollution.

She currently works with the CalEPA Assistant Secretary for Environmental Justice and Tribal Affairs, and Deputy Secretary for Science and Health on various public health issues of concern for environmental justice communities.

Dr. Galaviz, who also holds a position as an associate toxicologist at OEHHA, is continuing her work on several CalEnviroScreen projects, including acting as contract manager for a project with the University of Washington to evaluate air quality in San Diego County. Dr. Galaviz will present her research on urinary metabolites of 1-nitropyrene in the U.S. -- in U.S./Mexico border residents. So welcome to today's meeting, and we look forward to your presentation.

Thank you.

(Thereupon an overhead presentation was

presented as follows.)

DR. GALAVIZ: Thank you for having me here. And I am excited to talk to you about this study, looking at -- it's a community-based study that looked at diesel exposure using 1-nitropyrene and its urinary metabolites in persons at the U.S./Mexico border.

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DR. GALAVIZ: So the U.S./Mexico border is defined by the U.S. EPA as 62 miles north and south of the U.S./Mexico inland boundary, and extends into the sea boundaries to the east and west, as outlined by the red line in the image to the right.

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DR. GALAVIZ: So zooming in to the California and Baja, California international border, you'll notice there's currently six border -- six ports of entry. And to the furthest west is the San Ysidro port of entry.

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DR. GALAVIZ: Now, zooming into that port of entry, you'll notice that San Ysidro is bounded by the San Ysidro to the north, which San Ysidro is a district of the City of San Diego, and Tijuana to the south. And Tijuana is the largest city in Baja, California.

Now, this border crossing happens to be the busiest border crossing in the Western Hemisphere. And

this data that was collected was in 2010. And here, you can see the number of vehicle crossings in 2010, over 13 million crossings, and pedestrians, over six million pedestrian crossings in 2010, as well as over 70,000 buses that crossed northbound from Tijuana into California.

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DR. GALAVIZ: So if you zoom in further, of concern is the pedestrian pathway. And as you notice, to the image on the right, the pedestrian pathway is to the east of the 24 northbound lanes, and the six southbound lanes at this border. And their pathway is right within feet of the one bus pathway. And so these -- the commute time for the vehicles can average around two hours. And depending on the time of year, I mean it could go up to four hours. And so with the pedestrian pathway, their commute time also averages about an hour. And so these are idling vehicles next to these -- this pedestrian pathway.

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DR. GALAVIZ: And one thing I forgot to note on the image to the left, you'll see a red line going from Mexico into the U.S. And that is the pedestrian pathway. And that pathway, as you can see, can extend pretty far south as commute time gets longer. So what previous work has shown prior to this study was that occupational

studies have shown differences in diesel exposure between high exposure groups and low exposure groups, using either 1-nitropyrene or its metabolites.

There was also human studies showing that urinary metabolites of 1-nitropyrene were higher in participants with higher exposure to diesel. So one of the data gaps was can we detect a difference at the community level between a high exposed group and a low exposed group using both 1-nitropyrene and its urinary metabolites.

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DR. GALAVIZ: So the purpose of the study was to compare the personal samples of 1-nitropyrene to the urinary metabolites in the ability -- or in a high exposed group and a low exposed group at the community level. So what we did is we compared the urinary concentrations between border commuters and non-border commuters. And we also looked at the association between personal 1-NP and urinary metabolites using a multi-level linear regression model.

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DR. GALAVIZ: So for participant selection, we obviously had inclusion -- or exclusion criteria to account for any potential confounders. And so all participants had to be 18 years of age or older, they had to be non-smokers living in a non-smoking household, they

had to be free of any chronic conditions, they were not occupationally exposed to diesel exhaust, and they had to consent to IRB.

Now for border commuters, they had to cross the border at least two times a week or more as a pedestrian. And for non-border commuters, they were not able to cross -- they did not cross the border, any port of entry, in the prior four months.

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DR. GALAVIZ: So the samples that were collected, we collected 24-hour samples. There was two ways study members could participate, one was having a 24-hour time activity diary with a questionnaire and a spot urine sample following their commute northbound across the pedestrian pathway. The second way they participate was the same questionnaire, 24-hour time activity diary, a spot urine sample, but wearing a backpack with a pump that was connected to a PM2.5 filter that was able -- we were able to analyze for 1-nitropyrene.

And as you can see in this picture, it kind of gives you an idea of the backpack with the tube coming out and the impacter located near their breathing zone.

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DR. GALAVIZ: So this obviously presented a lot of challenges. I mean, it took us a -- about a year to

get approval to do the study from GSA and the Customs. And so it's an international border. It's high security. Imagine having -- being a participant wearing a backpack with loud pumps and tubes coming out.

(Laughter.)

DR. GALAVIZ: I mean, it's kind of nerve-racking. So in order to alleviate some of those concerns, I myself participated and did some pilot studies walking with the backpack, a loud noise, with tubes coming out across the border a few times. Nothing happened to me. Everything was safe. So it kind of alleviated our concerns that, you know, we were not going to, you know, potentially put these participants in any danger.

And so as you know, there are people that are concerned, you know, with any bomb threats that could happen, waiting at an international border. Not only that, but occupational safety with anything happening to the workers that worked there. So what we did is we gave them training about what the equipment was, if they were -- if they knew when a study participant was going to cross the border. They had fliers of the type of equipment. And if there was any concerns, I was there and at the border during the whole time any border commuter had to cross the border just in case.

And so an additional challenge was timing of

getting the urine samples. So these are people that are -- that cross the border mainly for work and/or school. And so their time was very limited. They were waiting in line for hours to get across the border. They have to go where they need to go. And so sometimes I was able to collect the sample immediately when they crossed, sometimes I had to collect the sample eight hours later after they crossed. So it kind of -- that became a little challenge, but, you know, we did what we could do with the study population due to their constraints.

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DR. GALAVIZ: So as a result, there was repeat participations. And the criteria for them to repeat is that three weeks had to pass from their last participation. So as a result of repeat participants, we had a total of 73 border commuters sampling events, and 18 non-border commuter sampling events.

And in total, there was 27 border commuters, and 17 non-border commuters. And all border commuters lived in Tijuana, and all non-border commuters lived in south San Diego. And they all self-classified as Hispanic.

The reported mean northbound vehicle delay time was 83 minutes, and it ranged from 32 to 137 minutes. And this kind of was an indicator of the amount of idling traffic commuter on the pedestrian pathway. And the

border commuters on average spent 60 minutes waiting in line to cross the border northbound, with a range of 20 to 200 minutes.

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DR. GALAVIZ: So in this slide, I just want to talk that with urine, we were able to analyze creatinine in a subset of the participants, because we had enough urine sample. It was not known if this was needed for these metabolites, but we did this as an exploratory analysis. And it was measured by the University of Washington's Hospital Clinical Laboratory using a colorimetric assay.

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DR. GALAVIZ: So in this study population, there was two metabolites that we were able to detect with reliability. It was the 8-OHNP and the 8-OHNAAP.

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DR. GALAVIZ: And here, shows you the comparison between the non-border commuters and the border commuters. So with both metabolites, we had a higher concentration in the border commuters than the non-border commuters. And with the sum of the metabolites, you'll see for both the unadjusted and the creatinine-adjusted, we had significantly higher levels, which shows you that having the sum of metabolites seemed to be a more robust measure.

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DR. GALAVIZ: With here, looking at the association between the personal 1-NP and the urinary metabolites, we saw that there was an increase of 1-NP for each increase of urinary metabolites. So we did -- this was done for all participants. So we combined the border commuters and the non-border commuters. And it was specific -- each urine sample was specific to that personal 1-NP sample. And we also -- this was done for the unadjusted -- the unadjusted urinary metabolites. But we found that the effect estimates were similar for the creatinine adjusted as well. And that this was also done with both samples being above and below the limit of quantification. And we found that the effect estimates were modestly attenuated when we excluded data below the limit of quantification.

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DR. GALAVIZ: So in conclusion from this, we were able to see -- we were able to see a difference in urinary metabolites between a high exposed group and a low exposed group at the community level, which hasn't been done before. We were able to also see that border commuters had higher concentrations than non-border commuters showing that they had higher exposure to diesel exhaust, whether from the border or from the background

concentrations of where they lived is another question that couldn't be answered here.

We had higher urine 1-NP metabolites associated with higher personal 1-NP exposures. But as Dr. Simpson had previously mentioned, you know, this only explains a small proportion of the variability between personal exposure and urinary metabolites.

And that concludes. Do you guys have any questions?

CHAIRPERSON BRADMAN: Thank you very much for the presentation Dr. Galaviz.

So we also again have 10 minutes budgeted right now for questions from the Panel about the presentation.

Dr. Luderer.

PANEL MEMBER LUDERER: Thank you for that presentation. That was really very interesting. My question has to do with the roadway traffic exposures for the non-exposed. What's the traffic density like around where they were living? I was --

DR. GALAVIZ: Well, so with the eligibility criteria for living in south San Diego to be the control group, you had to have similar population density as Tijuana, so only certain zip codes were allowed to participate. And one of them -- so San Ysidro is bounded by three major freeways. And so the traffic density is

quite high in those populations as well as the control population.

CHAIRPERSON BRADMAN: Dr. McKone.

PANEL MEMBER McKONE: I just -- you know, you're making progress. You have a model, right? I mean, the problem with this is we're still working in a qualitative way. I mean, in the previous study that we heard about from the miners and children and in this one, I mean, we're seeing the association. And your model seems like it could predict the association, but how far are we from actually predicting exposure going backwards from the biomarkers and having some reliable ability to say it's in this range or do you think we're ready to go there yet?

I mean this is kind of more an open question that we may save it till the end, but I think it's one that, you know, we always look at, like we're getting there. We're really getting close, but how close are we?

DR. GALAVIZ: Well, I mean, to have a strong understanding of being able to detect a biomarker, both at high exposure community settings, such as occupational, and low exposure community settings in the, you know, ambient concentrations, I mean, that's -- it's really important to have confidence in being able to detect these wide range of exposures. So all these studies together bring that confidence. But you're right, there is a lot

more to add to that model to help understand predictability. And that, of course, is going to come with a bigger study with tons more money to understand all these independent predictive variables that are necessary for this.

How far we -- how far away are we from that? I don't know. I think Dr. Simpson probably would be the best to answer that.

PANEL MEMBER McKONE: Well, that leads to a follow-up question is, so it's interesting, because, I mean, it looks like we could get there. I mean, we're not there yet, but I think that's an important point. It's with enough -- I mean, it's like any study, if you do it with 15 people, you'll see a trend, right, but you can't really say much. If you have 100,000 people, you can do a lot, right? You can -- making the analogy to epidemiology, but in exposure science, you know, once you have a large enough pool to do your calibration and really get the variability down, so you really think, I mean -- and I open this up again to others. I mean, are we getting to that point where if we got more people, more samples, more situations, we probably could get the variability down to where we feel like we can make predictions backwards from biomarkers.

DR. GALAVIZ: I think so. I mean, this pilot

study and others kind of give an understanding that there is going -- there is differences between different subpopulations, such as children and older adults. And also, not only that, but there's going to be within individual variability as well that we need to account for, such as genetics. So I think we're starting to get a better understanding of what type of predictive variable to account for, and then in a next bigger study.

CHAIRPERSON BRADMAN: Dr. Bartell.

PANEL MEMBER BARTELL: So I had just a quick comment in response to Tom's question to throw in here in the mix with inter-individual or intra-individual variability. The temporal variation in exposure, and its relation to the biomarker, I think is a really critical point that we should bear in mind.

And I think it's going to be very difficult to sort of use these biomarkers to reliably make connections with ambient exposures, until we actually understand enough about the pharmacokinetics to say what that temporal variability is in terms of the contribution. Because otherwise when we go out and measure a group of people, as we saw on the first study, you know, as we average over groups, we'll get very reliable indicators of group exposure. But if there's a short half-life, you're going to see wide variability over the same individuals

over time.

And I think that story has actually emerged. Dr. Bradman's written some papers on this with urinary pesticides, and biomarkers for those, which, you know, were actually used for decades and thought to be pretty reliable biomarkers, but it turns out they have very low intra-individual correlation over even relatively short periods of time. And we're even seeing that with some longer term biomarkers like mercury and blood during pregnancy, which actually also is poorly correlated across different trimesters of pregnancy.

And I've written on this and others have written on this as well, but I think part of the story that we really need to understand, in terms of interpreting that exposure versus biomarker relationship is how the pharmacokinetics affect the temporal variability in biomarkers.

CHAIRPERSON BRADMAN: Dr. Quintana, you had a question.

PANEL MEMBER QUINTANA: This one to follow up on that comment on variability. And so one obvious comment I guess is because the half-life of these metabolites were not known at the beginning of these studies, they weren't designed to have the best chance of finding a correlation between external exposures and metabolite. For example,

in the study, the exposure was a previous 24 hours, and based on the data that Dr. Simpson presented, perhaps a week's exposure would have been a better chance. And so some of the disconnect is the study design, I think, which might make it look less associated than if it was correctly matched, as we understand this more and more.

But I have to say that I agree that variability is an issue, but if we go back to the example of cotinine has a very short half-life. It's a metabolite of nicotine and it's used to indicate exposure to second- and third-hand smoke. The half-life is 17 hours, which is very short. And you might think, looking at pharmacokinetics and everything, this will be a terrible biomarker, because it's such a short half-life. But, in fact, if the behavior is stable enough, and the exposure is stable enough, even a short half-life marker can be very, very accurate.

And so it comes down to what is the exposure? If it's 24/7 at your house, perhaps the variability in the half-life will be less of an issue then if it's once a week you go see grandma and it's -- that's where you get your exposure, I guess.

CHAIRPERSON BRADMAN: Yeah, I think these are all very good points, and it's clear there's a lot of interest here in these studies on this issue.

Any other questions?

Maybe later on this after -- this morning, we can -- when we have more time for discussion, we can also kind of get into some of the issues around study design, you know, maybe we need to look at serial samples collected daily, and really look at some of those questions around inter- and intra-individual variability.

So I just wanted to clarify. It was just mentioned, but the air samples were collected for 24 hours.

DR. GALAVIZ: That's correct.

CHAIRPERSON BRADMAN: Okay. Yeah, I think you're right, Dr. Quintana, that -- because we had 24 hours of air sampling relative to a biomarker that might reflect a longer period of time, the actual, you know, 20 -- 15 to 20 percent increases in the model actually, you know, probably make a lot of sense in that it would have been greater if we had a longer time frame of air monitoring. I think that's a really good point, and just that this data also reinforces the value of this biomarker as an exposure metric.

DR. GALAVIZ: I mean, one more thing to note is that for the personal 1-NP sample concentrations there's a five-fold higher difference in border commuters than non-border commuters. So that's important to account for.

CHAIRPERSON BRADMAN: So are there any more questions from the Panel?

Okay. Then I think we -- thank you very much for your presentation. And we will have some more time to discuss these issues in more detail as we go through our next -- after our next presentation, looking at PAHs and I'll be introducing Dr. Luderer from our Panel for her work.

(Thereupon an overhead presentation was presented as follows.)

CHAIRPERSON BRADMAN: Dr. Ulrike Luderer is a Professor of Medicine in the Division of Occupational and Environmental Medicine at the University of California at Irvine. She is also the Director of the Environmental Heath Sciences graduate program. Dr. Luderer's research focuses on mechanism of action of reproductive toxicants, and on the roles of antioxidants and oxidative stress in reproductive toxicity and reproductive aging.

She has served on several national and international expert panels, such as the U.S. EPA Science Advisory Board, Environmental Health Committee, and, of course, our esteemed Panel here.

Dr. Luderer will present initial results from a Biomonitoring California laboratory collaboration that measured several PAH metabolites in women for a substudy

of Women's Health and the Environment.

So thank you. Enough of the formalities, and we welcome your presentation today.

PANEL MEMBER LUDERER: Well, thank you very much. I'm really excited to be able to share some the data from this laboratory collaboration with the Environmental Health Laboratory.

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PANEL MEMBER LUDERER: So the Women's Health and the Environment study, our long-term goals are to translate some of the findings of what we know about toxicant effects on the ovary from animal studies to humans and to look at ovarian dysfunction in humans. And so this was really a pilot study to demonstrate the feasibility of a larger study that we hope to do, testing the hypothesis, the genetic variations in biotransformation enzymes that are involved in metabolizing PAHs, modulate the ovarian toxicity of PAHs in women.

And some of what we wanted to test the feasibility of was -- one of the main things we wanted to test the feasibility of was using a micro-electronic dip stick monitor. So these are monitors that are sold commercially that can be used by women who are trying to become pregnant, and they enable you to get daily

measurements of two urinary reproductive hormones, LH, luteinizing hormone, which is in the main stimulus for ovulation, and the primary estrogen metabolite estrone-3-glucuronide.

And we wanted to see whether we could feasibly ask women to do that for multiple menstrual cycles, as well as doing home urine collection of urine samples for exposure biomarkers over multiple menstrual cycles as well.

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PANEL MEMBER LUDERER: So the toxicants that we were focused on in this pilot study and in the laboratory pilot collaboration are polycyclic aromatic hydrocarbons. So this is a little bit different from the last two presentations. We're not dealing with the diesel specific -- or more relatively diesel specific PAHs, but the other PAHs, the non-nitrated PAHs, the compounds that are produced by the incomplete combustion of organic materials, and some of the organic materials are shown here.

Let's see, it looks like the pointer is not working.

The food is food, meat, barbecuing, grilling, and smoking, burning tobacco, of course, is a well known source of exposure, burning wood, burning fossil fuels, as

well as exposure to hydrocarbon -- raw hydrocarbons as is shown here by the oil spill clean-up picture.

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PANEL MEMBER LUDERER: So just to show you the structures of the parent compounds of the metabolites that we measured, these are small relatively polycyclic aromatic hydrocarbons, naphthalene, fluorene, phenanthrene and pyrene. These metabolites -- the metabolites of these compounds and some of the metabolism of the phenanthrene is shown in the lower part of this slide showing you the three 3-hydroxylated phenanthrene and then analogous metabolism by cytochrome P450 also forms other mono-hydroxylated metabolites. And in this study, we measured three, the 1-, 2-, and 3-hydroxyphenanthrene.

So these hydroxylated metabolites of these small PAHs are excreted in the urine. And we know NHANES has been measuring these metabolites for quite some time, so we know that these are detectable in nearly 100 percent of Americans that were biomonitored in the NHANES study.

We also know that the larger PAHs, such as, for example, benzopyrene or dimethylbenzanthracene, which is often used in experimental studies, these are metabolized in analogous manners, but those metabolites are excreted predominantly in the feces. And so for biomonitoring you really don't find those in large proportions of the urine

samples. And so NHANES has been measuring these metabolites of the smaller PAHs.

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PANEL MEMBER LUDERER: So the ovarian toxicity of PAHs. Why are we interested in looking at PAHs on ovarian function?

So there's a wealth of literature from the toxicology data. I just wanted to briefly talk about some of that here to give you an idea of why are we interested in this question. So we know from rodent studies that polycyclic aromatic hydrocarbon exposure dose-dependently destroys the primordial and primary follicles. So primordial follicles are the ovarian reserve. There's a finite number of those. And when they're depleted, you have premature ovarian failure.

We also know that in utero exposure to benzopyrene, a particular PAH, decreases fertility and depletes germ cells in the female offspring. And we also have data in women, not about PAH data -- PAH exposure specifically, but about exposure to smoking, which as we know, as I just mentioned, is a major source of PAH exposure. That women who smoke also have earlier onset of menopause, and decreased fecundity. And that daughters of women who smoke, there are fewer studies looking at daughters of women who smoked, but they -- if their mother

smoked during pregnancy, that has also been associated with decreased fecundity, as well as earlier age of menopause in the daughters.

So that sets the background for why we're interested in this. But I'm going to be talking really about the exposure part of it today. And I hope to, at some point, be able to come back and talk about the associations that we found with ovarian function.

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PANEL MEMBER LUDERER: So overview of the study. So this was -- the participants were women residing in Orange County, California, who were 18 to 44 years old. They -- because we were interested in looking at reproductive hormones, they had to not be using hormonal contraception, have no history of surgical sterilization, infertility treatments with known ovotoxic -- treatment with known ovotoxic agents.

And so this was really -- this was a convenience sample. We had based -- at the base-line visit, a very extensive questionnaire that was really modeled after the National Children's Study questionnaire that was being piloted at the time, was administered. We obtained blood samples for ovarian reserve markers and biotransformation polymorphisms.

And then the women were given the home urinary

hormone monitor and instructed in how to use that, as well as the home urine collection kits. And then they were asked to do daily urinary reproductive hormone monitoring using these micro-electronic monitors, where essentially a woman identifies on the first day of bleeding in the menstrual cycle the window, which is a six-hour window during which she can -- would then be doing the urinary test for that cycle.

And the monitors are designed for commercial use, so they request -- they have an algorithm which decreases the number of days during which they actually request test sticks as subsequent cycles ensue. But the maximum number of days during the cycle that test sticks would be requested by the monitor would be 20 days.

So most of the data for the hormones will be coming from the follicular phase and the mid-cycle pre-ovulatory stage. We also asked the women then on cycle day 10, which is during the follicular phase, since most of the urine data for the hormones will also be from the follicular phase, we wanted the biomarker to also be collected during the follicular phase. So we asked them to collect urine on cycle day 10, and they aliquoted four vials totaling 20 ml of urine. And then we asked them to keep a daily diary that included questions on menstrual bleeding, smoking, medication, and alcohol use as well.

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PANEL MEMBER LUDERER: So the final study population, the data that I'll be presenting consisted of 51 women who completed sample and data collection for at least two menstrual cycles. So two of those women had two cycles of data and the remaining 49 women had three cycles of urine samples available for analysis of hydroxylated PAHs. We actually have many more menstrual cycles for which we have not been able to analyze the hydroxylated PAHs, but we started with the three, so -- and with -- the metabolites that were measured were nine hydroxylated metabolites of naphthalene 1 and 2, a hydroxy naphthalene 1-hydroxypyrene, 2-, 3- and 9-hydroxyfluorene, and 1-, 2-, and 3-phenanthrene.

And these are measured here by the CDPH Environmental Health Laboratory using isotope dilution gas chromatography high resolution mass spectrometry.

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PANEL MEMBER LUDERER: So this table shows the detection frequencies. And as similar as with NHANES, these are detected at very high frequencies in these women here from Orange County. 1- and 2-naphthalene were 100 percent in our sample, 148 urine samples from 51 women. We had sample detection frequencies greater than 99 percent. You can see for two of the phenanthrene and two

of the fluorene metabolites. And samples that had the lowest detection frequencies were still above 90 percent detection frequency.

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PANEL MEMBER LUDERER: These two graphs show the geometric means for the Women's Health and the Environment hydroxylated PAH measurements. I have naphthalene metabolites separated out on the right in a separate graph, because the concentrations are very different. These are in nanograms per gram of creatinine compared -- since our urine samples were collected between November of 2010 and July of 2012, we're comparing them to the NHANES 2011/12 geometric means for women.

And what you can see, just the general pattern here, is that in general these Orange County women had the geometric mean concentrations were lower than the same metabolites reported for women in NHANES during this period. But, of course, women includes -- also in the NHANES study includes a wider age range. So we weren't able to compare just for the age range that we were studying.

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PANEL MEMBER LUDERER: This table shows the correlations between the different PAH metabolites within these urine samples of these 51 women. One, I think the

key points that I want to make here is that the metabolites, if you look at 1-phenanthrene and 2- and 3-hydroxyphenanthrene, those are highly -- those were among the highest correlations that we observed, which is encouraging, since we -- they are metabolites of a parent -- same parent compound. And for fluorene, we see a very high correlation between 2- and 3-hydroxyfluorene and somewhat lower for 9-hydroxyfluorene.

You can see that in general all of these metabolites, even for different parent compounds were correlated with one another with the striking exception of 2-hydroxynaphthalene, which really had very low minimal correlation with any of the other metabolites, actually including 1-hydroxynaphthalene. So that's an interesting finding, and we can talk a little bit about what the reasons for that might be.

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PANEL MEMBER LUDERER: Because we had this unique opportunity where we had multiple repeated samples from the same women, we wanted to look at measures of within person variability, so one way of looking at that is looking at intraclass correlation coefficients. And there are various different ways of calculating ICCs. The idea here is that a 1 would be a perfect correlation that basically the three samples within women were identical

and 0 would be none.

And so what you can see here is that, in general, the correlations were relatively low. They were not extremely high for most of these metabolites, which if we're interested in looking at changes within women, for example, related to hormone secretion during different menstrual cycles, it's actually helpful to have variability, so that you can look at possible differences, for example, an anovulatory versus an ovulatory cycle in the same woman, how is that associated perhaps with the PAH exposures.

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PANEL MEMBER LUDERER: So what might be the sources of PAH exposure in this population. We have -- we know from other studies that the fluorene, phenanthrene, naphthalene metabolites seem to be very strongly associated with indoor air exposures. 1- & 2-naphthalene are strongly associated with smoking. And we've done preliminary bivariate analyses, and we also see that 1- and 2-naphthalene, although we had a very low rate of smoking, about 10 percent of the women smoked, they were in bivariate analyses smoking was associated with 1- and 2-naphthalene, as well as with two of the fluorene metabolites.

2-Naphthalene has also been associated with

traffic exposure and residents in an industrial area. So we all know that southern California has a high -- has a lot of traffic, and we've done some preliminary analyses looking at commuting, and we do see associations with commuting time with some of these metabolites.

1-Hydroxypyrene has been strongly associated in other studies with barbecued and grilled meat consumption. And we think that food -- in women who don't smoke, food is definitely a major source of PAH exposure. We unfortunately were not able to do food diaries for these women. The one, not food exactly, beverage that we looked at is we looked at coffee and tea consumption. And in the bivariate analyses, we are seeing associations between all of the phenanthrene metabolites, the 1-hydroxypyrene, as well as some of the FLUO metabolites with coffee and tea consumption actually.

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PANEL MEMBER LUDERER: So to summarize, nearly all of these Orange County women had detectable concentrations of the nine hydroxylated PAH metabolites, which is very consistent with the NHANES findings over the years. The geometric mean concentrations in these participants were lower than the geometric means for females in NHANES for 2011 and '12. And eight of the nine metabolites were highly correlated with one another, while

the 2-hydroxynaphthalene was minimally correlated with the other OH-PAHs. And the metabolite concentrations were not highly correlated across menstrual cycles within participants.

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PANEL MEMBER LUDERER: And so currently, we're finalizing analyses of the associations between the hydroxylated PAH metabolites and reproductive endocrine endpoints. And we hope to be submitting that manuscript soon. We have ongoing analyses of predictors of hydroxylated PAH concentrations in these women. And just throwing out there for discussion, since discussion is the next item on the agenda, I think it would be interesting possibly to measure 1 -- the 1-nitropyrene metabolites in these samples and maybe to talk about other exposure biomarkers of interest to measuring these samples.

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PANEL MEMBER LUDERER: And I wanted to, of course, acknowledge everyone that participated in the study, my collaborators, and, of course, support from NIH, as well as from the Biomonitoring California RFI. I'd like to -- be happy to take any questions.

CHAIRPERSON BRADMAN: Just a quick review of the agenda right now. We have 10 minutes budgeted for questions from the Panel. But then following that, we

have a much longer period for discussion around this. So maybe we should just limit it to informative questions right now. And then we can have a deeper discussion that would include all of the guest speakers and the Panel and also opportunities for public comment.

PANEL MEMBER McKONE: So these compounds -- these are the lighter PAHs, right? So these are going to be mostly volatile or not have a large fraction bound to particles or could be doing some of this -- depposition and remission, depending upon temperature and condition, right?

PANEL MEMBER LUDERER: Yeah, that's right. I mean, the other thing to keep in mind, I mean, these are used as biomarkers not only of the parent compounds, but also of the larger PAHs, which are not found in the urine because there's such a strong correlation. I mean, as you could see for these -- the four parent compounds that we were looking at, but also with the exposure to the other PAHs as well, which we can't really measure in the urine, so -- and I should also add that in addition to inhalation exposure being important for these, I also mentioned that for the 1-hydroxypyrene, in particular, food is a major source.

PANEL MEMBER McKONE: Maybe this goes to our discussion, but one of the things that comes up that were

-- for several of the PAHs is if you inhale them, right, they go through your system, and they can actually bind to a receptor before they get into the liver. Whereas, when you ingest them, they go right to the liver first. They tend to be more hydroxylated or they aren't prevented from being -- I mean, there is this pathway that could keep them, if you inhale them, you could keep them from being hydroxylated, if they -- if they have a pathway of binding to some protein receptor.

And I don't know how true that is for all of them. I think that happens for naphthalene. There's been some studies on the -- you know, the difference between the first pass through the whole body before you get to the liver versus the direct shot to the liver when you take it in. I don't know if that's --

PANEL MEMBER LUDERER: Well, the liver metabolizes these, but a lot of the target organs actually metabolize the PAHs as well. And the ovary certainly does, the lung. I mean, there's metabolism at the target organ as well as metabolism in the liver. I can tell you that with ingestion with oral exposure, the effects on the target organ that -- you know, that we're interested in, the ovary are very pronounced.

So there is a significant absorption of these compounds through the gastrointestinal tract, and

metabolism to the reactive metabolites at the ovary, despite the first pass.

PANEL MEMBER McKONE: Well, I mean, that makes sense, because they're both somewhat water soluble, but there's lipid uptake. And, I mean, if they're bound to lipids, they're still going to go into the gut. And these have -- even though they're semi-volatile and they've got -- they're probably dissolved in lipids and those lipids are absorbed, right, so they're going to enter into that pathway.

CHAIRPERSON BRADMAN: Dr. Bartell.

PANEL MEMBER BARTELL: Thanks for the presentation. It was very interesting. I was actually curious on one of the last slides where you listed what you thought might be other sources to PAHs in the population. You only mentioned the barbecued and grilled meat consumption for one of the metabolites, which was, I think, 1-hydroxypyrene, if I remember the name of that correctly.

PANEL MEMBER LUDERER: So -- yeah, go ahead.

PANEL MEMBER BARTELL: And I was just -- I was a little surprised, the Li paper, as you know -- may know, I was one of the co-authors on that, involved a single barbecue chicken dinner, and we saw 10-fold increase in actually all of these metabolites just between pre- and

post-administration of this single chicken dinner. And so I'm wondering just why it's singled out as only contributing to that metabolite here, because I guess my read just from these --

PANEL MEMBER LUDERER: They are -- yes, they are all associated. I think that was the one that was the most strongly associated in both of the studies. And so that was why I highlighted that, but, yes, they are all associated with exposure to barbecued and smoked foods. And it varies somewhat depending on what the foods are and what the method of cooking is as well, definitely.

PANEL MEMBER BARTELL: If you think -- I know that you're sort of already mid-stream in this study. Would there be any possibility to even retrospectively ask participants about their frequency of consumption? I don't think you'd get exact timing going back this far now. But, you know, in terms of how often each person barbecues, I think, you know, there's -- just a thing about the statistics. I think there's some ways you could even just incorporate that information to try to suss out, you know, some of the differences across individuals and within individuals over time.

PANEL MEMBER LUDERER: Yeah. I mean, that's something that I would really like to plan into a larger study. It was just something -- we tried to get some

funding to do it mid-stream while we were still in the process of collecting samples to see if we could go back and do that, but we weren't able to. But I am definitely interested, because I think that is going to be a major source of exposure.

PANEL MEMBER BARTELL: The serial sampling is really nice here to see too. And again something I think people have started doing in really just recent years. And I think that's really important. Obviously, in an epidemiologic analysis, it's actually useful to have that difference as you pointed out across subjects over time, if you're looking at short-term acute outcomes.

It becomes a challenge then if you're trying to assess chronic outcomes from, you know, a limited number of samples. But I think a lot of different lines of evidence are converging on the utility of actual serial biomarkers in the same individual so over time for a variety of research purposes.

CHAIRPERSON BRADMAN: Dr. Quintana.

PANEL MEMBER QUINTANA: I thought your comment that you see an effect of commuting very interesting, because one thing Southern California has as an exposure that you don't have some other places is spending a long time in the car and often not just in the car, but on freeways which are shared with big trucks. I think some

of the freeways are some of the most polluted in the world with diesel, like the 710, I think.

And so I think it would be very interesting to look at the 1-nitropyrene in those samples. If you actually are seeing with all the other sources that you mentioned already with diet, you're still seeing a signal from commuting. We do know that in-cabin exposures are -- contribute sometimes the majority of a person's exposure for that day, because of the small environment and the on-road emissions.

So it does seem to be a very interesting finding that you mentioned. It will be interesting to look at other markers, especially 1-nitropyrene.

PANEL MEMBER LUDERER: Yeah. No, I definitely agree. I was very excited by that preliminary finding too.

CHAIRPERSON BRADMAN: Dr. McKone.

PANEL MEMBER McKONE: I was actually quite fascinated that your geometric means were lower. I mean, that's -- were they significant? I mean, that's -- the importance of a geometric mean is kind of the anchor point of a distribution. And it's good. I mean, people look -- I mean, I don't -- so this is a very important point. It means that it must be systematically lower if your anchor point is lower.

Was it a bit -- quite a bit lower, and do you have a reason -- or a sense of why it might be lower?

PANEL MEMBER LUDERER: Well, you know, one thing that I could positively say is that this is a fairly -- you know, the population in the part of Southern California they were looking at, it is a fairly high socioeconomic status area. I mean, there is traffic, but, you know, I think it may have something to do with that where people are living versus where most of the traffic pollution is.

But I -- we're doing -- we're looking -- we have data on where the participants' home addresses are, and we have some work address information too. And so we're trying to do some modeling looking at personal exposure - and this is in collaboration with Jun Wu - to air pollutants and to try to see how well that predicts the biomarker concentrations we measured.

CHAIRPERSON BRADMAN: Dr. Quintana.

PANEL MEMBER QUINTANA: Not to keep harping on smoking and cotinine, but don't forget that NHANES is the whole U.S. And in California, we get used to our smoke-free everything. And it really is not the case in many other states. And so I'm -- I would just hazard a guess that some of that difference is exposure to even low level tobacco smoke.

PANEL MEMBER McKONE: Yeah, that was my suspicion. I mean, I just wanted to throw it out there, because it would be not only a difference in smoking, but also restrictions of smoking in most environments. It also could be diet too. I mean, we have somewhat -- particularly in Orange County, I think there's a sense of eating a different diet. I don't know how much you've looked at that, but that -- you know, there's probably less red meat consumption in this population than there is in the U.S. standard and intensely cooked food.

PANEL MEMBER LUDERER: I think that's likely true, yes. And we do -- one of -- we do have data on daily cigarette smoking for the women who smoked, but we have very low numbers of women who smoked. And so I agree that relative to the general population, I mean, California I think is the second lowest rate only to Utah in terms of female smoking, I think.

PANEL MEMBER QUINTANA: Just to clarify, I didn't mean active smoking.

PANEL MEMBER LUDERER: But passive exposure too, yeah.

PANEL MEMBER QUINTANA: I mean passive exposure because a little bit here and there does really add up, and it's noticeable in biomarkers. And then second-hand smoke causes an increase in these PAH metabolites in the

NHANES data.

PANEL MEMBER LUDERER: Right. And we wanted -- we do -- one of the possible things we could look at in the samples that we still have would be to look at cotinine. That was something we wanted to do, but we just couldn't do it with the pilot study funding.

CHAIRPERSON BRADMAN: So if there aren't any more specific discussions for Dr. Luderer, I want to then kind of open up for a broader discussion of the presentations we've had this morning, including all of the speakers. And I think we welcome input from staff and we'll also have opportunities for public comment. The goal here is really to think about what's been presented and what implications there are for additional biomonitoring work and perhaps health outcomes research we can do related to this that might inform the use of some of these biomarkers.

I should just say as kind of a personal perspective, and I've said this before, given how controversial and challenging the issues around diesel regulation have been in establishing a standard and the, you know, real economic implications for the trucking industry and commerce, I think there could be a real opportunity here to look at diesel exposures and kind of address our prioritization of diesel as a high priority

biomarker for the Program, and perhaps provide a service to the State by providing information about where the regulation is working and the importance of health benefits versus cost related to commerce, and perhaps ultimately come up with really a net win for the State.

And we have this time right now I think to talk about this. And I know all of us probably have some thoughts about where to go forward.

Dr. McKone.

PANEL MEMBER McKONE: Well, it would be helpful to me, I don't know about others, is that -- if we review what's in our list and what's out, because, you know, our list includes anything that's on NHANES, right, for the State Biomonitoring Program.

I mean, one of the reasons we're having this discussion is to also think about where we want to go next. But I don't think we have to add any of the PAHs that NHANES already does, because it's already on our list, but the 1-nitropyrene is not, right? I mean, that's the -- so one of the interesting things that comes up is we're still struggling to find a good marker for 1-nitropyrene. And that one I found, you know, particularly interesting that there's kind of a door opening here and how much we should explore that.

But, in general, I think it also does suggest we

want to revisit more broadly where we're going with the whole family of PAHs and various nitro-PAHs. Just a thought.

CHAIRPERSON BRADMAN: I think actually you raise some interesting points there. You're right, I mean, if we want to -- we have already designated diesel as a high priority. Can you -- Sara, can you confirm?

MS. HOOVER: Yes.

CHAIRPERSON BRADMAN: I think we basically said that diesel exposure or markers of diesel exposure are --

MS. HOOVER: Yes.

CHAIRPERSON BRADMAN: -- on our priority list.

MS. HOOVER: Yes. Sara Hoover, OEHHA. I was just trying pull up the footnote. Basically, when diesel exhaust was listed, it was listed as diesel exhaust with any bio -- you know, relevant biomarkers. So diesel exhaust is what's listed, which means that we can choose any biomarker that we wish to evaluate diesel exhaust exposure. So that's not an issue that Tom was raising about 1-nitropyrene. It's covered by the listing.

CHAIRPERSON BRADMAN: Right. And there's not necessarily a need to list that particular compound?

MS. HOOVER: No, there's -- it's listed. Basically, anything that we could identify as a reasonable diesel exhaust biomarker is already listed. It's covered

by that listing, and we specifically formatted it like that. I was just trying to pull up the -- I think we have a footnote that explains it, which I'll pull out in a second and read it to people.

CHAIRPERSON BRADMAN: So maybe the real question for discussion today among the Panel and speakers and all of us really is what -- given the information we have, where can we go forward to kind of inform the Program and the State about diesel exposure?

MS. HOOVER: Yeah, I'll just say, basically, this was discussed when diesel exhaust was put on the list. And the footnote simply says, "Diesel exhaust is a complex mixture that contains many compounds, one or more of which may be useful as an indicator for biomonitoring". So we can choose anything.

And just to -- I mean, I think Asa has some ideas for informal discussion questions. But to clarify what we mean about next steps, we're really talking about development of capability, you know, lab capability, design of studies, how would -- you know, going to the thing that you were talking about, Asa, regarding how we can provide a service potentially, you know, in demonstrating the effectiveness or maybe areas where it's not effective, you know, the diesel regulations, finding populations that might still be more highly exposed.

Those are the kinds of questions that would be interesting.

Also, the whole discussion on the variability and the half-life that seems like a really interesting angle to talk more about. So you don't have a practical matter before you today in terms of an official recommendation or any chemical selection issue, because we've already dealt with that. So it's really more about how do we go from here?

CHAIRPERSON BRADMAN: Dr. Quintana.

PANEL MEMBER QUINTANA: I think some of the most, you know, fascinating findings of today were looking at the difference, even with 10 children, which appeared -- was significant, but was very promising. That difference looked like it would be real if it were -- had more samples, so -- and in the interest of full disclosure, I'm a co-author with Dr. Galaviz and Dr. Simpson on the border crossing study. But that did show that air concentrations, differences in 1-nitropyrene were correlated with urinary differences when they're measured in the same individual.

So I think there's some pretty strong evidence that this marker could be interesting. It was fascinating to me how high the levels were in the children. And again, we do know that children absorb more from the same

environment than adults, and they're very much at risk from traffic exposures as shown by epidemiological studies.

So we didn't talk about this specifically, but my understanding was one of the issues that's been practical in the sense of urinary volume, so we use 10 ml -- 100 ml of urine for the border-crossing study, but I understand from Dr. Simpson that it was only 10 ml that were used for a study in the children, which is -- makes everything much more practical.

DR. SIMPSON: I believe that is correct, but I should defer to Dr. Bradman, that provided the samples. I'm pretty sure he didn't provide 100 ml per kid.

CHAIRPERSON BRADMAN: Yeah, that's correct. And that actually raises kind of a technical point that for us, you know, we had archived samples from the study. And, in fact, we even have some samples in these children collected repeatedly on a daily basis over two weeks. But, you know, these were young children three to five years old, and we did not -- 100 ml was beyond, you know, what we could spare, both in terms of maintaining our biorepository and not using up samples. And two, we just -- we didn't have that much.

So luckily, with 10 ml, we were actually able to get quite good detection frequency. But definitely

there's potentially a challenge there. But certainly getting 10 ml from kids is very feasible.

Dr. McKone.

PANEL MEMBER McKONE: I want to probe a bit more on this issue of the value of something like 1-nitropyrene metabolites. And what's interesting is it isn't a very long lived material, but for somebody who's exposed continuously, it's just going to be there. I mean, it's like -- I mean, when you're sampling something and there's a lot of variation, you probably -- you're probably going to see the baseline all the time. And then you're going to see a lot of variability, because there's peaks going up and down. I mean, that's a point we talked about with Dr. Bartell.

And I'm comparing the miners and the children, right, it really is interesting that the miners are lower, even though you would expect they get some short-term high exposures, but they may not persist well. And I know we're not supposed to know where this is, but I figured out where that mine is.

(Laughter.)

PANEL MEMBER McKONE: And I've been to that part of Montana, and it's absolutely beautiful air. There's not a lot of diesel exhaust. So it really reveals the importance -- you know, in some small scale for me it's a,

well, you could have a high exposure for a short period of time as a worker, but what's really going to show up in your urine and what really may matter is your baseline, what you're at all of the time.

And if you're in really pristine air of Montana with not a lot of diesel exhaust around, most of the time your home is probably pretty clean, then you might see that kind of effect. Because the children in Oakland near 880, that's a pretty heavily -- pretty heavy concentrations of all kinds of automobile and diesel exhaust in that area.

So anyway, for me, it kind of brings out maybe we can start using this -- this contrast to say well, you know, what doesn't make sense?

CHAIRPERSON BRADMAN: Dr. Quintana.

PANEL MEMBER QUINTANA: Just to follow up very quickly. It was also interesting that in Dr. Galaviz's study that these are people living in a fairly urban environment, but adults, and the absolute levels in the urine were very similar to the children's as well. And having been in that environment, I would suspect the levels are higher if you're standing in line at the U.S./Mexico border and in Tijuana with the lack of emission controls.

So again, we may be getting at children absorbing

be more per kilogram of child, as well as exposure differences. And that's extremely interesting from a progressive point of view.

PANEL MEMBER McKONE: Yeah. Well, just to -- so I -- and again, others probably want to come in, but I think it is pointing to the value of a much larger study. I mean, we do expect there to be temporal and spatial variability. You know, the spatial, particularly about where your baseline is. But if you have enough subjects and you're careful in the design of this, you could actually begin to learn how to use that to move toward a more predictive model. So it does speak to the -- I mean, I think there's -- like the door is opening and some light is coming in. And I think the best way to open that door more and get more light is to figure out a more systematic way to get all of the variability in there, and then learn how to use it to our advantage, as opposed to throwing up our arms and saying, it's uncertainty. I mean, if you understand your variability, it's not uncertainty.

PANEL MEMBER BARTELL: I agree entirely. I just wanted to kind of think about the big picture a little bit here too in terms of, you know, where the State prioritizes efforts. I would actually say, even though it's early in the development for 1-nitropyrene, I'm very enthusiastic about the possibility, just because in theory

this should be a much more specific marker of diesel exposure.

And if what we're really trying to get at is diesel exposures then we want a specific biomarker. Certainly, PAHs can reflect traffic exposure, but they also reflect a lot of other things as we've talked about, like smoking and diet. And that makes it very difficult to suss out for biomonitoring data what those mean in terms of, you know, effectiveness of interventions and regulations or decreases in one particular source.

And I think that's particularly true if there are questions about the extent to which diesel actually contributes to each of these PAHs, which I think we've talked about a little bit today. There's some debate, I guess, in the literature about that, but at least some evidence that in some cases that smoking and dietary exposures may actually be more important.

And so I'd hate to sort of have OEHHA putting a lot of effort into PAHs to try to, you know, capture diesel exposure when that may miss the target. And maybe we're already beyond that and already thinking -- already thinking in those terms. But I think for me that's one of the really exciting things about maybe trying to -- even though they're earlier in their development, maybe more in their infancy in terms of development of the science of

the newer biomarkers, like 1-nitropyrene. I think that's a reason to actually put some effort and resources into trying to bring those to maturity.

CHAIRPERSON BRADMAN: Dr. Luderer.

PANEL MEMBER LUDERER: I just really want to echo, I mean, I think it's very exciting that the 1-nitropyrene is so relatively specific for diesel. And that we can, using, you know, this biomarker, begin to sort out exposure to diesel from all the other exposures to sources of combustion that really play a role in the other PAH biomarker measurements. I think it's also though, I think, would be useful to measure them in the same people and in the same samples, because I think that would help us to start to get a handle of what are the different sources of exposure in addition to, you know, to the other -- in addition to the diesel exposures, what are other sources that are driving some of these PAH metabolites, the hydroxylated PAH metabolites. And I think beginning to dissect the diesel component versus the other component would be very interesting and valuable to do for the other PAHs as well.

CHAIRPERSON BRADMAN: I think we've -- I'll make one comment then Dr. Quintana. I think we've mentioned this before in the setting here, that we have some opportunities in California. We have almost a natural

experiment. For example, in the Bay Area, we have Interstate 880, which is a designated heavy truck route, and then we have 580 about two miles away, which also gets heavy vehicular traffic, but relatively low truck traffic. And we have a similar situation, I think with 710 and perhaps some other highways in Southern California.

So we have some opportunities to test some hypotheses about the importance of 1-nitropyrene. And then, of course, maybe with the -- any limited existing data we have, perhaps if we were to measure, for example, 1-nitropyrene in Dr. Luderer's samples, we have a few from Oakland now in children, we could link that to truck traffic data.

For the Oakland kids, we did have traffic density information. But from the data sets we had available, we're not able to take out -- you know, to really estimate truck traffic independently of car traffic. So it seems like that's maybe another step, if we have enough samples in that.

And I'm curious, maybe Dr. Simpson you know of other studies around elsewhere where they have tried to specifically separate, you know, truck traffic or diesel traffic from general passenger, car, gasoline based transportation?

DR. SIMPSON: So I confess I'm not aware of any

studies that have tried to do that using biological monitoring. There's certainly been a lot of work done using regression type techniques. So looking at predictors of car versus truck traffic on roadways and looking at things like relative contributions of nitrogen oxides versus black carbon versus ultrafine particles and things like that as predictors of exposure. And then using those air measurements and trying to associate them and epidemiology or cohort studies with different, usually acute, but also some chronic disease outpoints -- outcomes to try and differentiate the role of diesel traffic versus regular gasoline vehicle traffic.

CHAIRPERSON BRADMAN: Dr. Quintana and then Dr. McKone.

PANEL MEMBER QUINTANA: So I guess I have a practical question for Dr. Bradman and the Panel. So if we were going to move forward with it, I guess I haven't heard from the laboratory people in terms of just the technique and how they feel it would be doable or not doable. So I'm not sure if the laboratory people want to comment on that aspect of it. And also, it seems like I'm hearing from the Panel should we be looking for interesting populations to study, either within the ones that have already been biomonitored or looking outward within California, for example. I believe that USC

Children's Health Study has done some work on regression modeling for the truck versus car traffic, and have some archived samples, I believe.

So I guess I just have a practical question of where -- how do we proceed from here, if you could give us any direction, Dr. Bradman, or others?

PANEL MEMBER McKONE: Before we get to that level, I had a thought which was kind of along this line, but it's also -- we basically have a sense that 1-nitropyrene might be a pretty good marker. And, I mean, one of the -- but it might not be perfect, and there's going to be confusion and variability. And one of the things about information or information theory is that if you can get one reasonable good insight, and even a second lousy insight, it's more powerful than having one alone. Actually, it really enhances -- you know, this is the whole thing of group solutions of problems. Two people who don't know what they're doing, who work together, can get a lot farther than one alone who knows a little bit.

And I don't know -- you know, I mean, we've had this concern that there are markers of diesel exposure that aren't really good, and we weren't comfortable with them, because -- and now we're starting to get a pretty good one, but we might want to pull back some of the other ones that we weren't really happy with because they may

help us triangulate little bit and get more power to the one that needs -- I don't know what that marker is offhand, but we might want to think about whether there's a second.

MS. HOOVER: Hi. This is Sara Hoover OEHHA. I just wanted to briefly comment on what Jenny asked. We actually reversed our talks. We had our special session in the morning. You're going to hear from EHL. It's the first talk after lunch, and he will briefly -- Jianwen will briefly touch on the status of method development for 1-nitropyrene.

So the short answer is yes the Program is pursuing it. So again, in terms of talking about it today, we -- actually, at the -- you may recall in your materials we sent around the discussion from November 2014. At that time, the Panel recommended that the Program pursue trying to measure metabolites of 1-nitropyrene. And that's definitely still the intention and the goal.

There's just resource issues and equipment issues and staffing issues, that kind of thing. But that's being pursued and Jianwen will talk about it in the early afternoon. So I -- but I liked your idea a lot, what you highlighted about populations, you know, study design issues. Asa and I had talked about just brainstorming

some design questions. I think you could just continue along that path for this discussion, and then you can talk again about any method status issues after Jianwen's talk in the afternoon.

CHAIRPERSON BRADMAN: And to follow up on that, it seems like just from the discussion we've had a little bit so far, there's kind of some general feelings that, one, if there's studies with existing samples and data out there, there might be an opportunity to do new measurements on archived samples, which could answer some of the questions or address some of the questions we have. And then the next -- another piece would be what other kinds of new studies to do? But whether that would be exposure validation or perhaps it could be, you know, biomonitoring exposure study related to, and including an epidemiologic component. And then related to that is, you know, what communities in California should we consider studying?

You know, one idea that has come up in discussion is using CalEnviroScreen. And that includes measures of air quality. So we have actually -- you know, I believe EnviroScreen, we've been using it, it's down at the census tract level, but in some of those criteria, we can even go down -- drill down a little bit farther, but it's really an amazing resource that includes, you know, a lot of data

analysis across the state. And I think that could present a real opportunity to identify populations, to perhaps incorporate into a study or to do other kinds of monitoring.

So maybe that's something we should really talk about is, you know, what kind of communities should we focus on and what would be most beneficial to the Program in terms of where to go? And again, I still want to keep in mind this idea of, you know, given the investment in this state and on the private sector of trying to reduce, you know, diesel exposure, can we show that there's been some, you know, benefit from that investment?

I think both of you have comments, Dr. Luderer and Dr. Quintana.

PANEL MEMBER LUDERER: Well, I was just going to follow up on the -- being able to show the public health benefit of the changes in diesel engines and exposures to diesel-related toxicants. I think that it would be really nice if we could try to identify archived samples that are in an area -- geographic area, let's say we're talking about a place where we would potentially find high exposure, such as the freeways we were talking about with high truck traffic, or, you know, the Oakland children perhaps, who -- where we could have samples that were collected before the decline started, because I think it

was 2009/10 when we really started to see dramatic changes in the fleet.

Someone can correct me who knows this more than I do, but that would be, I think, really exciting to be able to show, you know, within the same geographic area, the same community, possibly before, and then continued -- you know, repeated measures, not within the same people necessarily, but within the same general population to really try to look at how that is impacted exposures to diesel exhaust with the changes in the engines and the truck fleet, et cetera.

CHAIRPERSON BRADMAN: Thank you. Dr. Quintana.

PANEL MEMBER QUINTANA: Yeah. So there may be also populations to do with goods movement at ports, so that's another big source of diesel. And I'm thinking of the Port of Long Beach, which had mandated reductions. Although we've been hearing the New York Times -- LA Times about how they've not been carried out to the extent at which they had planned, but -- and I'm not aware if there are archived samples, as you say, before and after.

I think one of the most exciting uses of the NHANES national data was showing longitudinal effects of policy changes, and even using the example of secondhand smoke, you know, reductions of more than two-fold between 1999 and 2010 in national exposure to, you know,

secondhand smoke.

And so I think a very strong use of this data is showing public health benefits, showing reductions that work, and I would support that very much.

DR. GALAVIZ: Can I say something?

CHAIRPERSON BRADMAN: Absolutely. This discussion is open to speakers.

DR. GALAVIZ: Vanessa Galaviz with CalEPA and OEHHA.

I just -- so one of the things that I looked at was some predictive variables. And one of the predictive variables that was significant was season. So in the wintertime, concentrations for both 1-NP and urinary metabolites were higher than in the summer, so just one thing to account for for next steps.

CHAIRPERSON BRADMAN: So I think the -- another comment down here? No. Okay. So why don't we -- it seems like we have a slight pause. And I think now would be a good time for any public comment that -- related to any topics we've talked about this morning?

So have there been any submissions for public comment?

MR. JACOB: Sorry. Tom Jacob with the Chemical Industry Council of California.

I don't have a dog in this hunt, but have been

fascinated by the discussion. I just had a question for Dr. Simpson. Relating to your mine data, I thought you mentioned something about respirators. And I'm just wondering the degree to which the folks at the mine face, in particular, would have actually been -- would have actually been experiencing exposure levels anywhere comparable to the ambient levels of it.

DR. SIMPSON: So there was only one task within the mine, where it was mandated that the workers were supposed to wear respiratory protection as part of becoming compliant with the lower MSHA standard for diesel particulate. A lot of the vehicles had emission control technologies on them, and a lot of them had enclosed cabs with HEPA filtration. And so the measured exposures on those workers would have been reduced due to those emission controls.

There was one type of vehicle where they were not able to do that. And those workers had to wear respirators. And so for specifically that group of workers, the personal air exposure measurement would have been -- or the relationship between that and biomarker would have been confounded by the extent to which they used the respirators and how effectively they used them.

So we did ask about that. In the questionnaire, we asked them to identify if they used a respirator and

how much of the time that they were exposed to diesel exhaust. They used it. And that was -- I believe it was one of the variables that we included in the predictive model.

CHAIRPERSON BRADMAN: We have some additional public comments. The first being from -- I see who has the microphone Nancy Buermeyer from the Breast Cancer Fund.

MS. BUERMEYER: Thank you very much. I just wanted to make a couple of points. First of all, we as -- we, as an organization, share the enthusiasm of the Panel and the Program of being able to find a way to track these exposures in connection to so many different health impacts including breast cancer, specifically with BAP. So thank for the work that all of you have done to pioneer these techniques.

The thing I wanted to call out, and you've got -- and the Panel sort of talked around it a little bit, but the implications of Dr. Simpson's research around the sort of cumulative exposure or cumulative presence, if you will, of the metabolites over a four-day period that's a discrete exposure, and what the implications of those increases over time are for the folks who are chronically exposed, particularly the children.

So like what's the pathway of exposure for the

children that are living near 880 or some of these other places, given what you've found with those sort of four-day exposures?

And the implications are pretty sobering, and I think something that we would be interested in looking at. I don't know how you look at it, except take children who move from Montana to, you know, Oakland and sort of track them over time from the moment they get there.

But anyway, I just wanted to pull that out as something that is very concerning, I'm sure, for all of us. And, you know, the environmental justice implications for this kind of research are significant. And as a person who does policy, the ability to show the impact of policy is one that we're always looking for, and I think this is ripe for that. So thank you all for the work that you're doing.

CHAIRPERSON BRADMAN: Then our next comment is from Veena Singla from the Natural Resources Defense Council.

DR. SINGLA: Thank you. Good morning. Veena Singla with the Natural Resources Defense Council. I wanted to second, third the appreciation of the work that was presented this morning, and to say that we also agree that it's very -- the Panel kind of discussed the need to move forward from the kind of pilot phase and into actual

implementation of these techniques for biomonitoring of communities.

And I would agree that the research should be focused on some of the aspects that are needed to move these techniques forward into actual implementation, because it would be very, very valuable for communities. And also to second what one of the Panel members said about looking at the Port of Long Beach and Los Angeles as a potential place to look at if there's archived samples, because I know our Santa Monica office has been very involved with both of those ports and the development of their clean air action plans.

And I'm not -- since I haven't been directly involved with that work, I'm not sure about the exact emission reductions that have been achieved, but it is my understanding that there have been significant emission reductions achieved at both of those ports, and that those could be good communities to investigate for looking at the policy effectiveness.

CHAIRPERSON BRADMAN: Do we have any --

DR. FLESSEL: Hi. My name is Peter Flessel. I used to attend these meetings all the time, but this is the first one in a long time.

I thought I would just make sure we hadn't thrown out the low molecular weight hydroxy nitroaromatics. And

I was curious to see whether you saw any in your searches for metabolites, in particular because of what Dr. McKone said about having two dumb people do a little bit better than one smart person. And maybe another marker from the low molecular weight nitroaromatics that apparently are there in two or three orders of magnitude greater concentration.

DR. SIMPSON: Thank you for that comment. So as you indicated, the nitropyrene metabolites are present in very low concentrations. In order to measure them reliably, we used a technique that basically shines the light specifically on those compounds. And so we only see the things that we're looking for.

That technique doesn't allow us to look at the low molecular weight hydroxy nitroaromatic compounds. And I haven't seen recently any additional work that's been done on the literature that's -- that has continued to explore those as a possibility. That's certainly a potential area of research for folks to look at with different techniques. But the method that we were using was blind to the compound that you mentioned.

CHAIRPERSON BRADMAN: Do we have any email submissions for the public comment?

DR. PLUMMER: No.

CHAIRPERSON BRADMAN: Well, so we still have --

we're running a little bit early, so we still have more time for discussion here. And I'm wondering maybe if we can kind of distill from this discussion some concrete recommendations. I know it's not our -- we're not making decisions here, you know, any formal decisions. But to summarize so far, it seems like, one, there's enthusiasm about 1-nitropyrene as a metabolite. And we'll hear more about the laboratory capabilities.

Two, maybe there should be kind of a RFI or kind of maybe formal attempt to understand what kind of studies and archived material might be out there that could be used at relatively low cost to inform the science related to diesel and 1-nitropyrene.

And then the other is to perhaps conduct new studies, and then maybe a question more for discussion is do we want to consider those studies in terms of exposure and health impacts and/or consider them also as perhaps representative of exposure, and as a way to show trends related to regulation. And those are kind of two different purposes, and they can overlap at some level, but they also could conflict.

So maybe it might be useful to have some discussion there about what would be more of a priority or how to weight them?

Dr. Quintana.

PANEL MEMBER QUINTANA: I had a couple of follow-up points. In terms of practical issues in proceeding, the variability in the markers has been brought up, and also the -- adding more, even if they're dumber markers. In this particular case, it might be looking at other PAHs, as well as the 1-nitropyrene, either oxy or nitro or parent PAHs in the same samples to see if they add any information. So that's some of the questions.

But I just want to point out something that I think Dr. Galaviz brought up, which was in her data that the sum of the metabolites was a bit more predictive than individual ones. And so if people have varying metabolic differences, they might go one pathway versus another. And it's been seen for other compounds, sometimes the sum of the metabolites can be more accurate than perhaps fixing on one, and so -- but it makes a lot of difference to laboratories, if they're measuring one of them versus a lot of them.

And so that's a non-trivial point to maybe think about as we go forward, should we ask them to just focus on, you know, the 8-OH one or should we, you know, have four of them that they're doing and then add them up, and see which one is better? It probably has some practical implications for the people in the laboratory. And also

for urine volume, I believe that maybe that it would take more urine to do more metabolites.

So just kind of a minor point, but it might help address those issues of variability, and so it may be worth doing, even though it's difficult. And the other question was to do with the other point. It was to do the CalEnviroScreen, you brought up using this tool to inform perhaps a selection of populations. And I believe that the later versions of CalEnviroScreen, Dr. Galaviz included traffic density in the metric, is that correct?

DR. GALAVIZ: Correct.

PANEL MEMBER QUINTANA: Yes, they did include traffic density as one of the variables that inform the most disadvantaged communities. And so do we have any archived samples that somehow map on to these communities would be a comment to follow up on your question about archived samples?

CHAIRPERSON BRADMAN: And, Sara, could I clarify, does CalEnviroScreen have an indicator that's specific for diesel?

MS. HOOVER: Yes. Actually, Vanessa you answer that.

DR. GALAVIZ: Yes, there is a diesel particulate matter indicator.

CHAIRPERSON BRADMAN: And how was that computed?

DR. GALAVIZ: So ARB actually computes this indicator for us. And what they do is a modeling approach. So currently, they have -- for example, they include both off-ground sources of diesel as well as on-ground sources of diesel. And based off of theirs -- those sources, they compute -- they do a model. And so obviously, there are some limitations to that to a modeling approach, but that's what they do.

CHAIRPERSON BRADMAN: And is it at the census tract level or is it --

DR. GALAVIZ: Yes, it's a the census tract level, correct.

CHAIRPERSON BRADMAN: It's at the census tract. So I'm thinking of our study. We probably have most of our samples collected within the same census tract, so it would be hard to look at variability. But possible to compare Salinas to Oakland.

DR. GALAVIZ: One thing like I -- you know, it is a modeling approach, so obviously the further away you get from having lack of data, you know, you're going to have much more uncertainty. But for the traffic density, it's much more -- it's not a modeling approach --

CHAIRPERSON BRADMAN: Right.

DR. GALAVIZ: -- so that might be a much more -- a better indicator to use.

CHAIRPERSON BRADMAN: Right.

MS. HOOVER: This is Sara. I just wondered, Chris, did you want to address the issue of urine volume for the sum of the metabolites?

DR. SIMPSON: Sure. So there -- I'll address two points that Dr. Quintana raised. So in terms of -- I think Dr. Galaviz shared data for four different nitropyrene metabolites. The analytical method collected data for all four of those compounds. And so the incremental effort required by the lab to quantify four rather than just one is probably not too great.

It's certainly the case that the data quality for the acetylated compounds is the analytical variability is quite a bit higher. And, in part, that's because those analytes, at least in some of the populations, were much closer to the detection limit, so the data quality is maybe not as good. But since the method can collect measurement -- data for all four of those compounds, I think you're right that it makes sense to process that data. And then in the subsequent data analysis, you can figure out how useful those additional metabolites are.

CHAIRPERSON BRADMAN: Dr. Luderer.

PANEL MEMBER LUDERER: Hi. In addition to identifying communities or geographic areas, you know, using a tool like CalEnviroScreen to perhaps focus where

studies might be done, I think it would also be very useful to identify maybe occupational populations that could be followed. And it might be particularly interesting, you know, things that come to mind would be diesel mechanics, perhaps dock workers, you know, drivers, bus drivers, you know, those kinds of populations with high exposure to diesel exhaust, and where we can look at occupational exposure and how the changes in regulations and the fleet are impacting in occupational exposures as well.

CHAIRPERSON BRADMAN: I agree that's important. It seems like there's a number of partnerships really that could be developed to look at this -- these issues in terms of academic groups. I'm thinking of Rob McConnell's group at USC that did a lot of traffic exposure, other children's centers around the State. We have, of course, our sister program at Berkeley that's working in Fresno and looking at asthma.

It seems to me there's some real opportunities here for both the academic and State and community groups to work together on this issue. And again, I just -- I think there's some real opportunities here to understand these exposures, and also answer real environmental health, public health questions, which are often challenging for those of us who work in this field.

Any more discussion?

We're running a little bit early, which is not a bad thing --

(Laughter.)

CHAIRPERSON BRADMAN: -- but sometimes -- I don't want to cut anything short. Sometimes you have to mull a little bit before we speak.

Dr. Quintana.

PANEL MEMBER QUINTANA: So you said earlier when you summarized where should we go from here? And I think you mentioned should we ask for an inventory of kind of samples we already analyzed and those partnerships, and maybe an evaluation by the staff of how informative it would be to analyze any of those samples that have existing partnerships, is that what I heard you say?

CHAIRPERSON BRADMAN: Yes, yes.

PANEL MEMBER QUINTANA: As well as maybe exploring new samples.

CHAIRPERSON BRADMAN: Right, right. I'm curious actually about if there's any -- might be some samples through the BEST projects through Kaiser that might be geographically diverse, and include both high and lower risk areas -- exposure risk areas.

DR. SIMPSON: Along those lines, and some of the Panel members are probably more familiar with this than I

am, but the -- there are some existing large cohort studies across the country that go back 10, 15 years in time. I'm thinking, for example, of something like the MESA study that has archived urine samples.

And given that the -- at least here in California, the diesel regulations have already had a substantial impact, in terms of reducing levels of emissions at least, being able to look at samples going back in time, and to determine whether the biomarker levels were higher back five, ten years ago when the emissions were higher, I think that would be a very valuable contribution to be able to make to the State.

CHAIRPERSON BRADMAN: Related to the issue of archive, since this came up when we used our samples, and maybe Dr. She we can discuss this this afternoon, but we mentioned earlier about sample volume, and we were able to successfully, you know, use about 10 ml for the samples from Oakland and Salinas, I'm wondering if there might be room for, you know, improvement there. I had an experience with CDC where they went from 4 ml to, you know, 500 microliters, half a ml, for pesticide metabolites. And I'm wondering if maybe with the progress in mass specs that we might be able to bring the sample volume down.

DR. SHE: Yeah. I look at the levels -- the

comparisons of PAH levels we found is most in 10 ppt levels. That's our current method detection limit, use 1 milliliter of the urine samples or two milliliters.

With the hydroxy metabolite and 1-nitropyrene look at the details around 0.1. So that's -- for our own laboratory experience, we need to push down the detection limit almost a thousand times lower. So that's maybe a reason I think Professor Chris use 100 ml. So then we only 10 times difference.

So with 100 ml, I think we will be able to do it. To push down like pesticide levels is almost impossible from what I can see. It's maybe with a new technology. The machine Dr. Chris -- Professor Chris used the EPI 4000. We have EPI 5000, which might give us a little bit of room, like a 10 times or five times more sensitive. But we do not have so much experience as Professor Chris doing it.

So that's a lot of the challenge, at least I see for us, if we do it ourself. We definitely need to work with Professor Chris to see we can push down our detection limit to 0.01 ppt levels, which seem to be a lot of work.

CHAIRPERSON BRADMAN: I definitely appreciate those challenges. When you look at the measurements, and then we're talking primarily in the picogram range, these are very low measurements in terms of concentrations.

So if there's not anymore discussion, maybe we should break for lunch early?

MS. HOOVER: Yes.

CHAIRPERSON BRADMAN: Okay. So we have -- we actually have, I think, an hour and a half scheduled for lunch today, a little bit longer. Originally, we were going to come back here at -- let me look at my schedule here. We're going to come back at 2:30 -- 1:00 to 2:30. So let's back that up and say we'll start back here at 2:00 o'clock, so we have -- yeah -- why don't we make it 1:45.

MR. HOOVER: Actually, yeah, this is Sara again. And Laurel has just informed me that, of course, we have a side lunch thing happening, and those lunches won't arrive till 1:00. So, yeah, let's not get too much earlier. So what did you propose?

CHAIRPERSON BRADMAN: Well, I would say 1:45.

MS. HOOVER: No, no, no. We're allowing an hour and a half. So even if we start now, it would be -- the earliest we'd come back is 2:00.

So we have actually an hour and a half for lunch scheduled, not --

CHAIRPERSON BRADMAN: Right, we were thinking of constrict a little bit, making it --

MS. HOOVER: No, no, no.

CHAIRPERSON BRADMAN: You don't want to do that?

MS. HOOVER: We can't constrict. There's plans for the lunch that require an hour and a half.

CHAIRPERSON BRADMAN: Okay. So why don't we say 2:00 o'clock.

MS. HOOVER: Let's say 2:00 o'clock, but remember before you break, read your announcements there.

CHAIRPERSON BRADMAN: Yeah. So we have to address the issues around the Bagley-Keene rules governing our discussion.

STAFF COUNSEL KAMMERER: Good afternoon. This is Fran Kammerer, an attorney for OEHHA. Because this Committee is subject to the Bagley-Keene Open Meeting Act, I would like to remind you that especially since there are luncheon events going on to refrain from discussing actually committee matters during lunch. And if you have a brilliant thought of one of the discussions, you had this morning, which were obviously very interesting, hold on to that thought, bring it back here. You'll obviously have an opportunity to discuss it. As Sara said, after the laboratory presentations, there will be ample opportunity.

So once again, hold that thought, don't discuss it over lunch, and come back here and talk about it and have a good lunch.

CHAIRPERSON BRADMAN: And I think everyone here is familiar enough, so you know what the options are.

We said we're going to start at 2:00. Let's have everyone arrive like at five to 2:00, so we actually get going at 2:00.

MS. HOOVER: Okay. Thank you.

(Off record: 12:28 PM)

(Thereupon a lunch break was taken.)

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

(On record: 2:00 PM)

CHAIRPERSON BRADMAN: So I think we should get started. I guess we're -- yeah, so we're going to call the meeting to order. I believe Dr. McKone will be back very shortly. So I want to welcome everyone back from lunch, and introduce our next agenda item, which will be focusing on laboratory updates. And first up is Dr. Jianwen She, Chief of the Biochemistry Section in the Environmental Health Laboratory Branch.

So Dr. She, excuse me, we look forward to your presentation.

(Thereupon an overhead presentation was presented as follows.)

DR. SHE: Thank you very much. Thank you, Dr. Bradman. Good afternoon and welcome to the members of the Panel and audience.

This afternoon I will provide the laboratory update for the Environmental Health Lab.

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DR. SHE: This includes staff changes, method updates, and ongoing projects, and our recent publications. As you know, laboratory didn't provide an update for last year. The last update we provided is in March 2015. My quick update, we'll include all of the

things that we have done since March 2015.

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DR. SHE: First, I'd like to introduce -- actually, I find out Ms. Su -- Ms. Su maybe already introduced by Dr. Mike D. in November meeting. So Ms. Su is visiting scholar from Shenzhen Food and Drug Control. She will be here with us for half a year. Actually, now next month she will be leaving. And she comes -- she have a lot of experience working non-targeted analysis, because non-targeted screening involved a lot of drug product, so she has experience. And she currently working with us on this non-targeted method development.

Another person I'd like to introduce is Dr. Yu-Chen Chang. And Yu-Chen was with us a long time ago, and then she rejoined us back about half a year ago. She's also tasked with non-targeted method development. We are very lucky APHL awarded us a fellow based on our application we submitted last November. The fellow also tasked by APHL, they want us to develop the new methodology to do the non-targeted analysis. We are in the process of interviewing the fellow.

Last on the items, we have two State limited-term positions. For these two limited-term positions, we're again in the process to recruit. I think that Dr. Chang and Ms. Su in the audience. If you don't mind, can you

stand up, so we can welcome you.

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DR. SHE: For the method update in last almost one year, we focus on the following four methods: One is the urine metal panels, and organophosphate flame retardants, BPA analogs, and non-targeted screening.

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DR. SHE: We changed the process of the urine method. The change, I mean, right now we use basic diluent, instead of acidic diluent. Why we do this is because we find the mercury tended to stick on the system, so you have the carry-over effect. If you run high level samples, like sample, may be effect. It take us a long time to clean up systems. Dr. Choi, he's in audience, he make this change.

So with this change, the mercury wash-out time was dramatically reduced, so that we also can improve our throughput. And the other benefit is we can lower our detection limits, and shorten analysis time I already mentioned. And by the way, we also -- with this process, we expanded our list of analytes to 13 chemicals.

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DR. SHE: I have reported in the past we are working on finalizing and validate OPFR method. For these four OPFRs we mentioned here, you can see them. Right

now, I can report to the Panel the laboratory did a very good result, and then we can start a project. So the next project that we try to do is work with ECL together to have some laboratory pilot samples. We try to do it.

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DR. SHE: Another group of chemicals the laboratory take on is BPA analogs, and mainly the para BPA analogs. The structure is showed here. And then with these five chemicals also we completed our method validation. We can do them also similar to the OPFR, we can get a very reliable result. These four extra additional chemicals. We also plan to use this method to do a pilot study.

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DR. SHE: For the non-targeted analysis, in the past, we reported to the Panel and the audience, EHLB is database, which includes more than 600 compounds, which we call the Toxic Chemical Finder. Toxic Chemical Finder database is one database we found. The strategy we try to test this new method with some chemical we already know, and then find a new one. The reason we do it, we need to make sure the new method at least can test the chemical we already know for sure is there. So to do that, we scale down a little bit. We build a more classical more chemical-structure related database, for example, like

environmental phenols that structure related. We already monitor some of them.

And then we can check how we're able to find new chemicals. So the example I show here is based on database we build around the benzophenones, like BP-3, this group of chemicals. We have over 70 chemicals. We build a database, and then we use this new method that we run. We find 17 compound matched with our database. This database include a lot of information. For example, they include the accurate mass of molecules, isotope profiles. So they also include the full scan spectra, plus a secondary spectra, which is a MS/MS spectra.

So the match -- I mean, that 17 compound matched with this four criteria, molecular mass, isotope profiles, full scan spectra, plus MS/MS. But we confirmed that they are the compound we suspect. We still need to purchase standard. If that's a standard there, we can find out. So the last step of confirmation, we buy some commercial available reference materials, and then run that one with this four MS criteria, and then match with the urine sample again.

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DR. SHE: For example, this is -- the first step, we test our -- the chemical we already know. We have traditional method, like BP-3, which we know how to do it.

We know how much is in the samples, so use this as a calibrator of our systems.

And the good news for example, we confirmed we find BP-1 in it, so -- also by checking the response levels, we notice the BP-1 is at least a similar level of the BP-3. So you can see from this example, at least for structure related chemicals, we can make some discovery.

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DR. SHE: When we further check the literature, we know BP-1 is a metabolite of BP-3, you can see that mythoxy group was changed to the hydroxy groups. And so this one is the one we confirmed. From 17 of them, we still have a few of them to confirm because their level may be low or the standard may not be available. We are still in process to process -- to process the data to see we can confirm more.

So, in summary, the non-targeted screening is working. We are help to help us to find the chemical we may not target on, which could be a predominant chemical in the urine samples.

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DR. SHE: I wanted to change the topic to see what we have on the project support part what we did. In last one year, we majorly supported three studies, one is PETALS, Pregnancy Environmental and Lifestyle Study. The

collaboration we did with Kaiser. And also Measuring Analytes in Maternal Archived Samples, MAMAS samples, and traffic related air pollutant study, which I already called it the Taxi Driver study. It is a collaboration with UCLA. It is more related to this morning's topic.

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DR. SHE: For the PETALS study, we -- from last time our reporting, we -- at that time, we only measured 60 samples. Now we have finished the 414 samples. Kaiser's PIs and her groups that did some studies. They're local This multiple sampling from same subject that look for the correlation or the ICC is kind of a parameter.

Unfortunately, we cannot reveal what that data is I think is still in preliminary stage. So we finish our around 400 samples.

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DR. SHE: The analyte for them is BPA, BP-3 and the triclosan. For the MAMAS studies, EHL's role is more like a feasibility study. Is this MAMAS samples collected for the Genetic Disease Screening Program is a serum samples. Are they proper, are they qualified to do the metals?

We've managed kind of different analysis we conduct. Our conclusion is at least for this six

compounds -- elements we listed here, this sample have a severe contamination issues. So you can see let's use chromium as an example on the most left five bars, the bank one is a control, which is a plasma samples. Without it, we put it into this serum collected tubes, so that the value is real value. But once you put it into the sample collection tubes, you think -- you see the value start to go up. Five days we test. Nine days, we test. We test 16, 26 days.

And we notice longer they stay in the test tube -- collection tubes, the value goes up a little bit higher. So we conclude for this six elements maybe not proper metrics, but the Program need to decide for the remaining chemicals, analytes, they need to continue this project or not.

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DR. SHE: So for the so-called Taxi Driver Study, the collaboration we did with the Professor Yifang Zhu at UCLA. Basically, they collect some samples from 22 taxi drivers, pre-shift, and post-shift. So you know according to Professor Zhu, there are around 4,000 taxi drivers in the L.A. area. And then a shift is about 4,000 people work 72-hours per week. And the shift of the work time is about six hours. So her goal is try to investigate exposure to PAH and the particulate matters like the PM2.5

or other particulates.

And also try to see if this PAH level or particulate matter have any relationship with lipid peroxidation. So she measured a lot of indicators for lipid peroxidation. So our EHL measured the PAH for her.

Totally, we measured the 232 samples. And second goal for her is try to see if she considered this an intervention study. She installed or changed the in-cabin air filter with high efficiency in-cabin air filters. Then she look for if this air filter have any impact on the exposure levels.

She summarized all of this what she found and sent it to the EHP for review. So hope that in the future, if we have more interest, she can provide a more detailed and more sound explanation for this study. I'm able to address some short questions of that related analytic part.

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DR. SHE: So this diesel biomarker method development is now go beyond a little bit of what laboratories currently experienced with PAH. So as you may remember in 2008, Dr. Peter Flessel he gave a group a first presentation. Within his update, he mentioned that, like Professor Chris mentioned, nitropyrenes groups, and then also he mentioned the PAH, combined with IGE,

combined with valid times, the other possible approach.

And then later on, last 2014, Dr. Chris Simpson gave a presentation and also Melanie Marty gave another presentation on the same topics. Laboratory did a little -- a preliminary preparation for these things, since this is almost eight years, why we didn't make a better progress.

One part is we concluded use 100 milliliter of urine at that time kind of a challenge for us to deal with. And we didn't put it as high priority. But since 2014, we established our direct contact with Dr. Chris Simpson. He provide us 14 standards, very hard to get a standard. I think he's the one -- he may be the only one to have it. He gave us a very generous gift and provide us 14 standards -- and 12 standards, which include some parent compound of nitropyrene and the metabolite and the isotope labeled standards.

So we have a foundation -- we also have the instrument to take on. If the Panel and the Program task us to do it, we can give exploratory work to see if we can make the method work. And also, we are very happy Dr. Chris Simpson is willing to help us to establish this method.

Other -- on the other -- on the negative side of this story is we -- CDC cut our fund last year. We lost

some experienced staff, even working on the PAH. Also, we operated with some limited term stuff. When the limited term up, people needed to find a permanent or relatively long-term positions that left us. We lost staff who has experience in working on the PAH.

So right now, we're not completely good to the point of zero, but we go halfway. We need to recruit people to reestablish this kind of experience on the PAH. And if we do the diesel, that's diesel on the PAH needed to be considered together.

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DR. SHE: Since March 2015, laboratory with the collaboration with other staff published the method. The first of five paper -- first paper is an editorial in the Environmental Health Perspectives. They tried to also spread the word, like China, you know, air pollution, they wanted us to write an editorial for Chinese audience about biomonitoring, so we did that. It's some more comment and editorial literature. And to help the other government to move on the program we are doing.

And next two papers majorly from our two previous visiting scholars. The second paper is about benzene and toluene exposure biomarker. You can receive from the titles. And the third paper is another Shanghai CDC visiting scholar. And he did some work in China.

And the number 4 paper is a report of a focused study. We find a high level of BP-3. And this is the Program's collaboration. And also, we work with Dr. Kim Harley and also Dr. Asa Bradman's group. We did the HERMOSA Study. This paper is in EHP in press.

And thank you for your attention, and I'm open for questions.

(Applause.)

CHAIRPERSON BRADMAN: Okay. Thank you for that presentation. We have a few minutes now for the Panel to ask any questions or -- sorry. Again, we have some -- a few minutes right now for any questions or clarifications from the Panel?

PANEL MEMBER BARTELL: I guess I'm a little concerned about what I'm hearing that, you know, the loss of one or two people, you know, is that big a setback for the laboratory. Could you give us -- did I understand that correctly that you have basically a very small staff, and so, you know, you lose some expertise if even one or two people leave, make it difficult to come back to the capabilities to measure was it PAHs, I think?

DR. SHE: Yes, for the PAHs specifically, we have had some time -- some time when we lose staff, we have enough overlap, we are able to train the staff and take over. For example, we started with Dr. Bob Ramage. He's

the one that started the PAH. And then he promoted to -- he left us. And then we have Dr. Simon Ip, and Anthony Zhou then take it on, so that didn't cause a leave for us to maintain the capability.

But last year -- no, the year before, 2014, in October, Dr. Simon left us. And then Anthony was transferred to a different unit. And then this majorly put us actually on hold about the PAH. And we still maintain the machine, maintain the instrument, but currently we do not have a staff to work on the PAH.

We also stopped the participation of the CDC PT program, which is a checking performance. So this new hire will try to address this, so at least we can first step train this person to do the PAH, which look like a little bit easier compared to the one with nitro hydroxy-PAH, because the level is almost 100 times difference.

PANEL MEMBER BARTELL: Yeah, just, I guess, a comment. I mean I think you guys are doing a tremendous amount of impressive work with, you know, a relatively small amount of resources here. And I don't know what the solution to this is, but I guess it's a concern to me to hear that, you know, you're sort of operating right on the edge of sustainability, because I think we'd all like to see this become a clearly self-sustaining effort at the

State level.

DR. SHE: Thank you. Yeah, that's also exactly one of our concerns.

CHAIRPERSON BRADMAN: Anyone else have a -- Dr. Luderer.

PANEL MEMBER LUDERER: I just wanted to say it's always -- it's really nice to hear an update on the non-targeted screening, because that's certainly been something that, as a Panel, we've been really interested in -- you know, in having the Program -- in suggesting that the Program pursue for a long time. So it's great to see that you're making progress in that area with this example of the benzophenones.

CHAIRPERSON BRADMAN: So that was a good introduction to my question. I actually had a question about the non-targeted screening. So I wanted to clarify, was this an example where you had an unknown urine sample, and you essentially screened it for a number of peaks, and then went back and tried to identify them using, you know, for example, mass spectra libraries? So in other words, there was -- you were not -- you didn't have any prior information on what was in the urine sample, and then successfully identified the unknown peaks.

DR. SHE: Yeah. This is very generic urine samples. We do not have the previous information on the

BP-1, which ones we found. But we know for sure must have the BP-3, because most urine we work have BP-3 in the past.

CHAIRPERSON BRADMAN: Right.

DR. SHE: So this actually you are right, so we run minimum sample process steps to make sure all of the chemical supposed to be there stay in the samples. And we do not -- wanted to run a very strict sample clean up. They may be gone. So then we run the samples through the -- we call the data acquisition procedures, and then we look for the database to find out. So this -- this is a semi-target or non-target. We target it with a wide database with a class of chemical. We didn't target with individual chemicals. So from this class, over 70 of the chemicals we find this chemical.

CHAIRPERSON BRADMAN: Right. And then would a possible next step be to kind of compare the -- say, the mass spectra and perhaps even the retention time against some standards?

DR. SHE: Yes, that's a very good point. The last step to confirm this MS information alone is not enough, so the general approach scientific award -- except they either compare like you said with the real retention time and the real samples of MS characteristics. So that you can see we did it with -- we did last step. We

confirm the in-house mass spectra library of commercially available reference materials, which is a standard.

So basically for BP-1 we know for sure it is it, because we have the real compound to compare. Another accepted identification criteria is using an MR program. We don't have it. Also, they require more sample to do it. Sensitivity not as good as the MS, so we prefer to buy standard to confirm it.

CHAIRPERSON BRADMAN: Right. I'm just curious, are there any of these compounds that you identified where there aren't standards available, so you could have a situation where you might identify something likely through, you know, a mass spec library, but really be unable to confirm it?

DR. SHE: Yes, that's really like -- if the light -- chemical itself was unavailable, and then you run very new chemicals, that's -- two ways you can try. One is you may find a substructure of chemicals, because through the library search most of the times they matched is a piece of it. They may not match the whole structure. We call it substructure identification. So from that substructure, you can guess what kind of group of chemicals there are.

Also, the MS they have certain rules. The chemical goes through the mass spectrometer just like go

atmospheric chemistry. They have certain ways to breakdown. MS is very destructive. They provide about 20 EV, so some bonds may have broke down first. Based on the bond energies, there's some theory to predict, okay, this chemical. If you -- this bond broke down, you put a piece back, you can guess the original structure.

Because the last is dependable, but it's with a lot of experience you can try to propose a structure of original chemical. And also some software program that will predict the -- if you have this chemical, what kind of breakdown you have. So from two paths, you can suggest a structure for it.

CHAIRPERSON BRADMAN: Right. Okay. Thank you. And I think this is -- like Dr. Luderer said, I think this is a great beginning looking at untargeted compounds. And think I'll probably look forward to hearing more about that.

Anymore questions or clarifications from the Panel?

Well, I think then perhaps it's time for Dr. Myrto Petreas to provide an update on the Department of Toxic Substances Control Laboratory work.

Thank you, Myrto.

(Thereupon an overhead presentation was presented as follows.)

DR. PETREAS: Good afternoon, everyone. As Dr. She said, it's been a year since you heard any update from the labs, so I'll cover what we've done at DTSC.

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DR. PETREAS: So basically I will cover changes in staffing, where we stand with our major projects, which is the California Teachers Study; our plans for other upcoming studies, and as I usually do, I'll mention some DTSC activities that benefit the Program indirectly.

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DR. PETREAS: So the good news is that with the 2015 budget, we got funding, limited term, but we're able to form the Biomonitoring Branch. And Dr. June-Soo Park, over there, he's our new Branch Chief, which is great, because now we can consolidate State and CDC funded staff under him, and it's much more productive. So it's limited term. We hope it will last and take advantage of that.

The bad news is that Dr. Erika Houtz, funded by CDC for two years, decided to leave for better salaries in the private sector. And we have been recruiting, even made some offers that were turned down. So I think our salaries are not very competitive. But we'll wait until we find the right match. So we have two CDC funded positions, now we only have one, but we're moving along.

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DR. PETREAS: So a little bit about the California Teachers Study. What I'm showing here is the map with, I guess, addresses of the women who participate at the time of joining the study. This is a very big prospective study of over 130,000 women who are members of the State Teachers' Retirement System.

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DR. PETREAS: Overall, the Teachers Study, which started in 1995, does an annual recontact process, and there are also periodic questionnaires every two or three years. In addition, there's access to databases, like the Cancer Registry, and the mortality and hospitalization databases to assess the health status of the participants. So this big, big effort was initially supported by State funds, but now they rely on federal and State research grants. That's the overall study.

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DR. PETREAS: So we got one of the research grants from the Program a few years ago. And we're working with the Cancer Prevention Institute of California, which is the lead, UC Irvine, and City of Hope. And for this study, we are recruiting and drawing blood from a little over 1,000 cases and 1,000 controls from the entire State.

We completed recruitment in 2015. It was very

slow. It took longer than we thought. Fortunately, we got a no cost one-year extension for the study. And we're really working hard to complete the analyses of organochlorine pesticides, PCBs, PBDEs, perfluorinated chemicals, and also thyroid hormones and lipids.

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DR. PETREAS: So the major objectives of this substudy is to screen for major predictors of PBDEs looking at behavioral factors and sociodemographics, along with variables of indoor and outdoor exposures. And the second objective is to assess persistent organic pollutants as risk factors for breast cancer.

So to do that, obviously we need to complete the case control -- collect all of them and do the case control analysis. What we plan is Dr. Reggy Reynolds who's the PI from the CPIC, we'll plan to have her give you a presentation more of the overall study and our specific aims in one of the -- probably one or two next SGP meetings.

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DR. PETREAS: So in the meantime, where we are in the lab as of this week, we have received over 3,200 samples, but we decided to stop at the numbers you see here, everything that was extracted at the time. So a little over 2,000 samples have been extracted for PFCs,

and almost 2,200 for the PBDEs and PCBs and pesticides. And through each of these silos down, we're moving, they're competing instruments and resources, but we're making progress.

And so far, we have released data of 1,600 PFCs down to almost 800 pesticides and PCBs. But the plan is to catch up now and complete all the chemical analysis to proceed with the statistical analysis.

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DR. PETREAS: So while we're waiting for the case control analysis, we also have some preliminary data that we'll look into. First of all, in collaboration with the City of Hope colleagues, we provided them samples that we had characterized for the chemical content, and they used a novel bioassay they have developed to estimate overall estrogenic activities as a potential intermediate risk factor for breast cancer.

This lead to a publication to which we are co-authors. But more importantly, it led to another award from the California Breast Cancer Research Program to look at menopause as transition and window of susceptibility for the promotion of breast cancer by environmental exposures.

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DR. PETREAS: And Dr. Chen from the City of Hope

is the PI. Under this award, we, the lab, are going to analyze additional samples, about 150 serum samples for PBDEs and 600 for PFCs. So that's where we stand with the Teachers Study planning.

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DR. PETREAS: We also looked at some data, and it is very interesting. Residential proximity to solid waste facilities in association with PBDE levels. So there's a publication in press at ES&T coming out this week or so.

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DR. PETREAS: Basically, we looked at controls, 932 participants without breast cancer, and accessed information from the Solid Waste Information System database from the State of California, identified the close to 1,600 facilities that are utilized to receive, store, separate, convert, transfer, or otherwise process solid wastes.

So looking at where -- if you remember, we had the location of the residences. Everything is geocoded, so we know where people live and we know where these facilities are.

So the interesting thing is that we found that compared to participants who live more than 10 kilometers away from a facility, those that live the closest, within two kilometers, have 45 percent higher BDE-47 and BDE-100

levels. Those living between two kilometers and 10 kilometers had 35 to 30 percent higher.

So there's a gradient, and this is the first time we see that. We know that PBDEs are really indoor exposures. So it's the first time that we see that this -- we know PBDEs are transferred by, you know, long range transport, but how can this affect, you know, your serum levels in your home is something which is really intriguing.

And I should say that we have a seminar this March 23rd. It's open. It's a webinar. People can participate if you want to ask questions. Ruiling Liu, the first author, will be presenting the work. I mean, questions like is it socio -- is it a surrogate for socioeconomic status. Those are different things that she looked into. It's very interesting.

So if you -- you can use this slide to register, if you want, or you can contact me for more information on that. So that's with the Teachers.

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DR. PETREAS: We're getting ready for the second phase of the MAMAS, which is Measuring Analytes in Maternal Archived Samples. Essentially, a biobank of serum samples for pregnant women from throughout the State. We have completed the analysis from the first

round, which were pregnancies of 2012 from Orange County and San Diego Counties.

And now, we have received and we're ready to start analysis of pregnancies that happened in 2015 from different counties, north and south. For this study, we plan to analyze PBDEs, PCBs, and pesticides in serum. And for the first time, we'll use our expanded polyfluoro and perfluoro chemical analysis to -- which we can encompass 35 analytes rather than 12 in serum. So we're eager to see what this will look like.

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DR. PETREAS: Another study that is very interesting and starting, it's underway, is the Foam Replacement and Environmental Exposure Study, or FREES. It basically tries to answer the question, do exposures change if sources are removed?

So in collaboration with UC Davis, the Environmental Working Group, Green Science Policy Institute, and the Silent Spring Institute, we're almost done recruiting about 25 participants who are willing to replace their furniture.

A side study, an additional, is to -- we're attempting to recruit about 10 participants from affordable housing, with the Green Science Policy Institute helping subsidize the furniture replacement as

an incentive to participate.

The way the study is designed, we have questionnaires, you know, time zero, and sampling at baseline, and then at 6 months, 12 months, 18 months. The idea is that once you remove your foam furniture to see whether things change.

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DR. PETREAS: So in the lab, we're ready to analyze samples that we have from in serum, PBDEs in serum, and OPFRs, the phosphorous flame retardant metabolites in urine; in addition, PBDEs, other BFRs, OPFRs in foam removed from the replaced furniture, and also hand wipes at different stages again.

UC Davis will be analyzing the dust. And in a week from now, we have a seminar that Rob Voss from CDPH will discuss the study and give more information. Again, this is something anyone can log in and register and attend the webinar.

I should say that the FREES study is of high interest to DTSC's Safer Consumer Products Program, because of the obvious testing here, that if you remove -- if you can reformulate a product, what happens, can you lower exposures?

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DR. PETREAS: Okay. So as usual, I'll give you a

few of the other activities, DTSC projects, that are not funded by Biomonitoring California, but indirectly complement the Program.

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DR. PETREAS: So some years ago, we had reported very high PBDE levels in California breast milk. That was from women who participated in 2003 and to '05, way, way in the beginning. Of course, we had found record levels and we published that.

In the meantime, there was a legislative intervention and which led to the phase-out of PBDEs. So we thought can we see any effect of that? So we decided to repeat the study in 2010 and '11, and this time recruited 67 women. Similar demographics, used the same protocols, but we only worked with one of the facilities, one clinic in Santa Rosa. So we had more access and more consistent protocols with the staff there, because in addition to the breast milk, we collected cord blood at birth and also maternal blood.

So I should say that both studies were partially funded by U.S. EPA Region 9 and we're grateful for that.

So what did we find? So if we can compare breast milk between the two periods, this is what we saw.

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DR. PETREAS: So red is the first period, green

is a newer period and you can see significant drops. This was just published in Chemosphere.

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DR. PETREAS: So what we saw is there was a 39 percent drop in the sum of PBDEs between the two time periods. On the other hand, every breast milk had PBDEs, so babies would be exposed. And, in fact, 30 percent of the babies would be exposed to BDE-47 above the U.S. EPA reference dose.

The good news is that in the previous study, 60 percent of the babies would exceed that same reference dose. So overall levels are dropping and the fraction of highly exposed babies is dropping, but still we have quite a ways to go.

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DR. PETREAS: Nevertheless, that was of very high interest for our Department. So last week, we had a press event with our Director, Barbara Lee, which she's quoted here stating that, "This study shows that regulatory and public health intervention works. The new findings underscore the importance of biomonitoring studies, and highlight the concrete benefits of product reformulation". That's from the Sacramento Bee article that came the next day. So it's nice to know that Director Lee appreciates biomonitoring studies.

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DR. PETREAS: In addition, very recently, the second study, not only breast milk, but in cats. Again, a similar idea. We had published the paper where we found high levels of PBDE in cats. These are the dark columns. And as you can see, the second time, both times were after the phase-out, but we see a time trend. So whereas, the PCBs and pesticides did not change between the two periods, there was a significant drop of PBDEs, between the two periods.

And moreover, when we look at the PBDEs in cats with -- who are hyperthyroid and cats that were not hyperthyroid, the ones which were hyperthyroid had higher levels. So that was an interesting paper, and it's coming out -- actually, it's out in ES&T just this month. So pretty consistent results.

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DR. PETREAS: PBDEs are dropping in California. It's consistent with some other -- with the phase-out of PBDEs from the furniture. And we can support that, because we are involved in the -- in a side project in supporting the Department of Consumer Affairs in enforcing the new labeling law, SB 1019, which every new piece of furniture now will have a label indicating whether it does or does not contain flame retardants.

So in preparation for that, we received a lot of these kind of products, we analyzed, and we didn't find any PBDEs. We hardly find bromine in those contemporary furniture pieces. A lot of other things, you know, but that's beyond the point.

So furniture doesn't have so much PBDEs now. And our data on dropping PBDEs in the breast milk is consistent with our previous findings. Actually, the first time we reported a drop in human blood was in 2013 in collaboration with UCSF.

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DR. PETREAS: And the question is we see that PBDEs are dropping. We're not sure if they will continue to drop or they will reach a plateau, like the PCBs have done.

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DR. PETREAS: Because, if I show you here, this is a collaboration with UCSF. And the first two bars are the data we use for the Zota paper showing 39 percent drop between 2008 and three years later. Now, the third phase, which is exactly the same, second trimester, maternal serum, there's not so much of a drop. So we're not sure if it's something -- is it that the two periods, the second and third period are too close together or something is happening and things don't change that much?

So there's more to do and we'll have more information in future presentations, where both Dr. Park and I can both or either of us present additional material here. And with that, I'll leave you.

And if you need any information about our seminars, if you want to be on our mailing list, contact me and we'll put you there. We have good webinars. So with that, are there any questions, please?

(Applause.)

CHAIRPERSON BRADMAN: Thank you for that presentation. It was really fascinating. I think the information on changing levels in PBDEs in humans and in house cats is really just kind of data that really helps us understand, you know, whether policy interventions really work. And I think that's so valuable.

So, Tom.

PANEL MEMBER McKONE: Yeah. This is really interesting work, and it's encouraging to see the PBDEs go down. I guess I have a concern that there are substitute flame retardants that were going in during this time, that some of this is just going down because there's -- industry was switching before changing was switching to the organophosphates and are we watching those? This is probably a broader question than just for you, but, I mean, are we watching the other flame retardants?

DR. PETREAS: Yes, we are.

PANEL MEMBER McKONE: Okay. Great.

DR. PETREAS: I mean we're watching not only us, but others as well. We're watching with the products, first of all. So, yes, as PBDEs were dropping Firemaster and other bromo -- brominated flame retardant was coming up, then the TDCPPs, the organophosphates are coming up.

So we know what's happening in the consumer products. We know what's happening in dust. There were studies reported where PBDEs are dropping, but of course, these other chemicals appear in dust higher.

Now, those classes are not measurable in serum. So PBDEs we can measure in serum, but the OPFRs have to be in urine and some of the Firemaster, mostly in urine. So it's not something we could measure in these type of studies.

We know that by the time we did our study, industry had already moved to new chemicals. And the classes we know were measured in the appropriate matrix. But the data pattern tracks, we cannot measure at the same time.

CHAIRPERSON BRADMAN: Dr. Luderer.

PANEL MEMBER LUDERER: Thank you for that presentation. Very interesting as always. I have a question about the PBDE concentrations and the -- I was

noticing that the cat levels seem to be particularly high. And I'm wondering do we think -- do they have an idea whether that's related to their being closer to the ground and more exposure to dust and licking their fur or does it have anything to do with metabolism?

DR. PETREAS: Both. So we know that cats cannot metabolize, cannot glucuronidate. So there's something in the metabolism. And of course, they're closer to the ground. They groom themselves. They're good sentinels for little children, of course. But you're right, you observed that -- you have a good eye observing differences in concentrations. I remember the morning.

(Laughter.)

DR. PETREAS: Yeah, so much higher levels in the cats.

CHAIRPERSON BRADMAN: Any other?

PANEL MEMBER LUDERER: I want to highlight what you just said, that -- the point that they might be good surrogates or models for children with the, you know, hand-mouth contact, and being on the floor. So that obviously -- maybe -- I don't know whether you have any biomonitoring studies ongoing or samples that could look at these levels in children and see how they're decreasing over time as well. That would also be very interesting.

DR. PETREAS: I think we'll talk about some ideas

for monitoring children in the future. Yeah, next presentation.

CHAIRPERSON BRADMAN: Anymore comments, questions clarifications from the Panel?

Okay. I guess thank you, Myrto, very much.

I guess we'll then move on to our section of the comment. At this point, we have an opportunity for -- well, there's potentially an opportunity for Panel questions, but right now I think we should have -- invite any public comment on what's been presented since we got back from lunch. So if there any submissions, let us know. Are there any submissions from the web?

DR. PLUMMER: No.

CHAIRPERSON BRADMAN: No public comments?

This is a time when we miss Davis Baltz, who was --

DR. SINGLA: I have a comment, but I don't have a mic.

Thank you. Veena Singla with Natural Resources Defense Council. I wanted to thank Dr. She and Dr. Petreas for those very informative presentations. And I also found the flame retardant results that Dr. Petreas presented very interesting. I was particularly alarmed by the higher PBDE exposures to folks living closer to solid waste disposal sites. I think that highlights the legacy

problem that we do have with the PBDEs, because it's estimated that there's still about 70,000 tons of PBDEs in use in products in homes in Canada and the U.S..

So there -- it's estimated that there will be ongoing exposures to PBDEs, even though they've been banned and phased out, because of the large stock of in-use products. And I think of the communities near waste and disposal sites, also recycled products that contain PBDEs are definitely a concern for exposures, because the -- as Dr. Petreas pointed out, the levels in breast milk are still a concern, even though they're dropping, and the communities with higher exposures would likely be higher than those levels of concern as well.

MS. BUERMEYER: Hi. Nancy Buermeyer with the Breast Cancer Fund. Again, thank you to everyone.

I actually had a question and I'm not exactly sure who to ask it of. But in thinking about some of the other flame retardants that are out there beyond PBDEs, I was in some meetings this week where people were talking about challenges in identifying exposures to TBBBP, which we, I think, are all exposed to, but I think it's been difficult to measure in biomonitoring studies.

So is that true, and are you all working on developing methods specifically to TBBBP? It's a flame retardant. I'm looking. Yes, I'm sorry. TBBPA. Sorry.

That's why I had all these confused looks coming my way.

DR. PETREAS: Myrto Petreas, DTSC.

Assuming we're talking about tetrabromobisphenol A, TBBPA, that's a chemical that used to be used a lot as a reactive chemical. So it was well bound to plastics, or the television sets and the backing. We're hear -- and so once it's well bound, it doesn't escape, it doesn't migrate so well.

Now, we hear that it's been used instead of PBDEs even in foam, in some other material, and it's an additive, so it could escape. So until this information came up, nobody had paid too much attention to TBBPA in humans. And we had measurements in dust and some products, but I think this is one of the things we need to investigate. We have not so far.

DR. SHE: Like Myrto mentioned, many of the newer flame retardants may end up or the metabolites in the urine. Instead of like the legacy ones, PBDE, which is persistent, tended to be in blood. I believe TBBPA, if they really go through the metabolism program -- process, that may end up in urine, put them in the non-targeted screening as a first step, maybe one option.

CHAIRPERSON BRADMAN: Any comments, clarifications of the Panel? Anymore comments from Program staff.

Okay. Well, I just, I guess, wind this up now. But actually I want to thank Veena for your kind of calling out the issue of higher PBDE exposures closer to solid waste facilities. I mean, actually thinking about that, that's a very dramatic finding. And if that holds up, you know, that's actually really important. And 10 kilometers is pretty far. So we're talking about potentially a lot of people living close to solid waste facilities, whether it's a transfer station or some sort of disposal.

It's hard for me to actually think about the mechanisms by which PBDEs would get out of a facility and into the neighborhood, other than maybe, you know, dust or some -- you know, some other mechanism, or perhaps, you know, fugacity, to finding the pathways where it moves through the environment.

But I'm actually -- I hope I can participate in that -- listen to that seminar, but if we can't, I'd be certainly interested to hear more updates about that, and look forward to the article that's coming out in ES&T.

PANEL MEMBER BARTELL: A quick question. Were those going to be on-line seminars?

DR. PETREAS: Webinars.

PANEL MEMBER BARTELL: Webinars. Thank you.

CHAIRPERSON BRADMAN: So if there's no more

comments then from the

DR. PETREAS: Yes. Webinars.

PANEL MEMBER BARTELL: Yes, webinars. Okay. Thank you.

MS. HOOVER: Yes, it's an on-line webinar.

CHAIRPERSON BRADMAN: All right. So I think we can then move on to the next agenda item, which is the --

MS. HOOVER: Asa, so no last -- no further Panel input or discussion in general for ECL or EHL, anything about the lab updates, just double checking?

CHAIRPERSON BRADMAN: Okay. I kind of hinted at that, but are there anymore general comments for the labs?

PANEL MEMBER BARTELL: I just -- I have a question that would be helpful for me as someone who's still relatively new to this Panel. Is there sort of a clear demarcation of responsibilities between these two labs? Because it strikes me that, you know, there's potentially some overlap in the kinds of things you would measure, or do you just decide sort of on a case-by-case basis for these studies which lab is going to handle the analyses?

DR. DiBARTOLOMEIS: You haven't heard from me yet today. So this is Michael DiBartolomeis. I wasn't around at the very beginning of this Program, but there is demarcation between the two labs. It kind of splits where

persistent chemicals, and those in blood would be in the ECL lab, whereas urinary metabolites, as well as metals would be in EHL.

The one major deviation from that is just fairly recently where the flame -- the organophosphate flame retardants is a method that both labs developed for different reasons, but we now have -- that's the only method I know that we're -- where we're overlapping. And this was something that I assume was just decided by the -- early on, because of either previous experience in the laboratories or some decision making that that occurred earlier on in the Program.

CHAIRPERSON BRADMAN: Any other Panel comments?

I mean, I guess -- sorry, you kind of prompted me to think a little bit more generally. And, you know, one comment I had is that Dr. Petreas also raised concerns about some loss of staff and some funding issues and challenges filling vacancies. And we haven't really talked about the financial status of the Program for a while. You're going to? I was going to say --

MS. HOOVER: Good segue.

CHAIRPERSON BRADMAN: Well, with that --

(Laughter.)

CHAIRPERSON BRADMAN: -- I'll introduce Michael DiBartolomeis, who's the Chief of the Exposure Assessment

Section in the California Department of Public Health and leads Biomonitoring California.

(Thereupon an overhead presentation was presented as follows.)

DR. DiBARTOLOMEIS: Thank you, Asa, and hello, everyone. I'm in that enviable position, I think, of being the last speaker of the day. So I'll either command your attention, because you know if I don't finish, you'll never go home.

But I am going to do something quite different, not only from today's presentations, but just different in general. I haven't even given something like that -- done something like this before.

So let me just kind of reflect a bit, and spend just a minute to reflect a bit. We're all here because we have common goals, common interests, whether it be public health, environmental protection, children's health, the chemistry of chemicals and the toxicity of chemicals, justice, environmental justice. I mean, we have common goals that we all share.

But what's different is that each one of us is here through their life path. They got here -- we got here in a different path. We're here for slightly different reasons maybe, choices we made earlier on our lives, so our life and professional experience are quite

different.

In thinking about this session today and that knowing that we were going to go last -- or I was going to go last, staff have -- the staff urged me to pull away and do something a little different, which would be, since we all have stories to tell about how we got here, Michael, what is your story; how, and more importantly, why are you here; and how does that relate to the direction that the Program is going, since theoretically I'd have some kind influence on that? And based on my past experiences, what do I see that -- where this Program is heading that would address some of the things that I saw as I was growing up and becoming older?

So if you can indulge just for a little bit, I'm going to tell you my story. And I hate to say this, but, you know, it was a dark and stormy night -- no.

Actually, it does start with me growing up in the -- in a wicked small town outside of Boston with three sisters. And I had no brothers. And early that wasn't -- early on that wasn't a problem, because when you're two or three years old, and your older sisters are torturing you, you just have no clue that they're actually torturing you.

But as you get a little bit older, you realize I should be doing things apart from that. And I started to explore the world outside of my little sibling situation.

And I was lucky enough to grow up and live in a yard that had a beautiful backyard.

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DR. DiBARTOLOMEIS: This is not it. But I did have about an acre of woods in the backyard. And I started going out there on my own and finding my little spots, my sanctuaries where I could escape and hear the bird song, and smell the fresh air, and just enjoy the trees. And this is back in the sixties. And just really became a part of nature.

And my mom encouraged me to go to camp and do this sort of thing, and explore the outside world. As I got older, I went outside of the backyard and started exploring the neighborhood, and then eventually the State of Massachusetts, and then the country, and even internationally.

But one thing always struck me and bothered me. And it was something that has stuck with me ever since, and that is it didn't matter where I was outside of my yard, wherever I walked, no matter how far away I was from houses and urban sprawl and all that, I found trash, trash on the side of the trail, trash in the river, trash along the seashore. And trash became an obsession of mine. I started literally picking it up and packing it out wherever I was, and had just really became obsessed with

trash.

And the other thing that was happening in the early seventies, and I know there are some people here old enough to remember this, we started seeing a lot of photographs of polluted air in L.A. and Lake Erie with brown water, even Charles River. So pollution -- the visual pollution was a very -- was very important, and had reached a point where the government started to take action.

So there was a very visible world out there that was removing that pristine environment and replacing it with something that humans have treaded on, humans trespassed. And this is going back to my childhood. Why did I see trash, why did it bother me? It's because I thought I was escaping from that sort of world where there was a lot of these external influences, where I wanted to be one with nature.

But seeing those cans and beer cans and all that stuff, brought me back to that point where I was saying humans have trespassed on this area.

So I got to college, and I was -- I started college with the thought that I was going to be an M.D., because that's what my father wanted me to do. I wanted to be an architect, but that's another story. So I took the usual classes one takes in pre-med. And by the time I

got to my sophomore year, I realized I wasn't going to be an M.D., because I didn't really like organic chemistry and it didn't really like me either, and I was kind of in limbo.

And so my first future ex-wife actually handed me a piece of paper. And it was a seminar lecture notice for a lecture on toxicology. And, okay, that sounds good. I don't even know what it is, but it sounds good. Because remember, this is back in 1973 or something like that or '76. And I went to the lecture, and afterwards I had this Eureka moment. I said, I can go and become a toxicologist, go to grad school, you know, get all -- do that sort of thing. And then I can wear a badge that says I am authorized to clean up this stuff. I'm authorized to go out there and clean up the world.

So I pursued that path, and got my degree, and eventually ended up in State service. And it was quite different than I thought it was going to be. I thought I really was going to be an environmental pollution police or a cop or something. It turned out that it was -- it's much more theoretical. And up until -- really, when you think about it, a lot of the work we do is very theoretical, chemistry is more -- much more applied, but then again when you're trying to figure out what is safe, what is not safe, you tend to do -- work a lot with the

theoretical.

And I really hadn't felt completely fulfilled, but I was -- but I felt like at least I was contributing to the basic science around pollution.

Well, I would say that around 2012 or so, Michael Lipsett came to me and we started talking about the Biomonitoring Program. And I had been involved in biomonitoring back even when Peter was -- oh, Peter is gone -- but, you know, the discussions early on about setting up a Program in the State.

And I realized that we see pollution and we can maybe convince people that the air is polluted or that the water is polluted, but inside of our bodies, that's invisible. That's pollution that's in our bodies that you can't see. And how do you explain to people that your inside is a reflection of what's outside as well. I mean, what goes in is, you know, in a lot of cases, stays in.

And I started connecting the dots. Maybe, there's still a chance that I can be that pollution cop and this time expose what's in people's bodies that they can't see, and make them realize that this trash that's in their body needs to be cleaned, and it needs to be -- and we need to stop putting it in there in the first place.

So with that, I come to you, and that's why I'm standing here. The reason why I'm here is because I

thought I would be able to address those inside our body pollutions with biomonitoring because it is a very powerful tool to expose and divulge what is -- what are in -- what's in our bodies.

So how does that relate then to the Biomonitoring Program? What do we -- what are we going to do and how have we been doing, and what are we going to do into the future 2016 and beyond to address some of these issues of the trash that's inside of our bodies?

Well, I'm going to talk about that.

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DR. DiBARTOLOMEIS: So you've seen something like this before from me. I've done it in different iterations, and this is evolving. And it's fair that it does evolve, because as we hear from the SGP and from the public, and as we do our own research, we're going to want to advance different ideas as we move forward.

So none of this is totally brand new. Although, some of the concepts that we're pushing now are a little bit newer.

So in terms of the general mandate, of course, we have the statewide surveillance. And let me break this out, so we can --

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DR. DiBARTOLOMEIS: So it is our primary -- one

of our primary mandates. And you know all too well about the BEST study, the Central Valley study. That's more or less looking at a randomized population with Kaiser Permanente. And the MAMAS samples which you've heard about from the labs earlier, that's also mentioned to get at more of the statewide surveillance. We're not satisfied. And for obvious reasons, this is not going to get us at the bigger question of what's trending in the State and what would be a background level, et cetera, in the State.

But you also know of our funding issue. So we're not able to do the type of study that one might want to do if they were to design it like an NHANES, or something along those lines, but we do think we have other ideas for collecting specimens by doing more mobilized collections, rather than having them be archived. And amongst that, that might involve bringing children in to biomonitor.

I'm going to speak a little bit more about children in a second. And with these kind of samplings, we can actually nest other types of studies in, so whether it be an intervention or a consumer product type of emphasis. And we can also couple our statewide surveillance with environmental monitoring. This might be important, for example, if we were asked to look at a community that might have high lead exposures, or

something along those lines, where you can do water monitoring and biomonitoring.

So this is really not a new thing, but it definitely fits in with the context of looking inside of our bodies and being chemical detectives to see what is in -- what is in Californians bodies.

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DR. DiBARTOLOMEIS: We've talked about consumer products in the past. It's a very important collaboration with the Department of Toxic Substances Control that we work together to look at what kinds of products might be contributing to the invisible pollution in our bodies. And obviously, there would be an opportunity then to set policies and do regulatory action to take action to actually change what might be a formulation in a product.

The FREES study, which we've already heard about today, this afternoon, is one of those such studies. It's really a pilot. It's not a large study, but we're actively pursuing it. We're hoping that in a year from now somebody will be able to stand here and give some, you know, preliminary results, for example, to see what might be happening. But basically, that's, you know, an important priority that will help us get at some of the things that are really important for us.

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DR. DiBARTOLOMEIS: We've talked about interventions. We've heard, let's see about a year ago or so. I can't remember when Kim Harley was here. But when we heard about the HERMOSA study, that's like a prototypical intervention study perfect for biomonitoring. It's small enough that you can do it with a reasonable -- within a reasonable time frame, with reasonable resources. That involved community, so you're having -- you're actively educating as well as involving community.

And on top of it all, there's a quick policy result there. Wow, you take these chemicals away and these products, and you'll see a reduction in these invisible chemicals, and therefore there's an immediate action that can be taken.

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DR. DiBARTOLOMEIS: Those of you who know me know that I come from a -- also a background of environmental justice work, back -- all the way back into the early 1990s. And this is a really important aspect of our work in biomonitoring as well, because not only are we interested in how populations and communities might be disproportionately burdened by external chemicals or chemicals from the environment or consumer products, but it's also important again to involve communities in these studies, to get them to understand what they can do, what

kinds of -- by learning about these things how much power they would have to -- and how much their voice becomes louder in the forum of politics.

We do have one study underway, which is the Asian -- let's see the ACE study. I don't know if we've actually mentioned this yet, or if it's come up really briefly, but it's the Asian and Pacific Islander Community Exposure Project. We are pretty much still in the early stages. We're still in the IRB stages and in developing some recruiting protocols, et cetera. But we -- this will be well underway. And this is an EJ context project where we're looking at Asian populations where they -- for certain chemicals, mainly metals, and I think it's perfluorinated chemicals.

Thank you.

And these -- and partially with the survey instrument we'll be using, we'll be looking at diet and exposures that might be specific to this community.

And, of course, we've also talked about how we would use existing databases, such as -- and approaches such as CalEnviroScreen and Environmental Health Tracking. So EJ and biomonitoring really go together like peanut butter and jelly, so I think we're going to be seeing a lot more moving forward with EJ emphasis, and incorporating this concept into our planning.

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DR. DiBARTOLOMEIS: Finally, as promised, we're -- this is something new. We have always talked about children and how important children are in developing children, and to be able to track chemical exposures early on in a person's life. And we haven't really partaken in these types of studies as a biomonitoring program. And a little bit -- partly, it might be because of having to rethink a little bit about collection of samples and those sort of things, partly because maybe the recruitment aspect is a little bit more difficult.

But we do think that, at this stage, we should be at least piloting such a study. And I think this is going to be further -- there will be further discussion as this year rolls on. And I think we already have some interest on the Panel for pursuing this. I look at Dr. Bradman, for example, because we've heard that before.

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DR. DiBARTOLOMEIS: And then finally, as we've heard from the laboratories today, it's not just continuing with a routine analyses of chemicals, we have to keep expanding our methods. We have to keep advancing them. It's really important that we stay ahead. As chemical products change in their formulations, as the

ratio of chemicals change in the environment, we have to be ready and willing, if we're going to continue to be detectives, to explore new methods, to look for new chemicals in our bodies.

And we talked about targeted and screening unknown chemicals, but we also have panels that can be expanded, phthalates, for example. There are other phthalates that we don't have in our panels. And we can also create new panels as needed. But obviously, as you will see in the last part of my presentation, we do have some challenges.

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DR. DiBARTOLOMEIS: Well, you asked me for an update on funding. So I just happen to have an update on funding. First of all, our current budget still is -- we still have a very -- a steady level of State funding. We -- and I want to correct one thing that Dr. She had mentioned earlier. I don't know if anybody caught it, but he said that we received a cut in CDC funding. I want to clarify, just so you all -- I think you all know what I'm going to say, but we actually had a five-year grant. At the end of the five-year grant, which was August of 2014, we were awarded a new grant from CDC for five years, but the maximum award level was significantly less than the original maximum award level.

Even though we received the maximum award level, it's significantly less. And I think that's what Jianwen was referring to took when he said we took a cut. But technically it wasn't a cut. It's -- but it is a reduction.

The State has been trying to figure out ways to compensate for that, but we're still -- it's a constant sort of annual struggle to even compensate just for the federal fund reduction. And it doesn't really speak to the fact that the funding for the Program has never been optimal in the first place. So I think that answers maybe, Scott, where you were -- I think you had a couple questions about that.

And we have created an optimal budget plan for the Program. It's off the shelf and ready to go if anybody wants to actually start thinking about ways to get money into the Program, but we do know what it would cost to have an optimal program, and what the components would be. I'm not prepared to give that presentation today, but you never know, maybe it will come up in the future.

Staffing. Again, you've heard a little bit about the staffing problems and challenges from the laboratories. They are real. Part of it is that when you have temporary positions at lower salaries, it's difficult to recruit. We still amazingly draw really good people to

the Program, and we are able to maintain some really good people here, but it's difficult to recruit, especially if, you know, as I said, they're temporary positions, and then retaining them. Retaining them if they are finding that they can't live in the Bay Area, for example, on the salaries they are, they're more apt to find a competing salary somewhere else that they're going to jump to, or because the positions have temporary nature to them. They're -- something -- a new opportunity comes up that's permanent, they're going to be leaving.

So retaining -- and promotional opportunities are really hard to come by too. So just retaining staff makes it really difficult as well. I'm not complaining. These are just challenges. And we have overcome them, but there -- it's at a cost. Sometimes we're not moving as fast, sometimes we're not able to develop those advanced biomonitoring methods as quickly as one would like or to be able to go into areas which would make a lot of sense.

Collaboration. It's a challenge. It's one of those things that -- it's a happy thing to have as a challenge, because anytime you do have a successful collaboration, it's not one plus one equals two. It's like one plus one equals five. I mean, you really do have a synergistic and exponential kind of growth, when you have a good collaboration.

But some of the issues with collaboration are, for us, for example, we were not able to fund a collaboration per se, so we would need to have partners that come with their own funding or were able to bring funding into the Program, and, you know, wow, I'm sure we're the only ones looking for that kind of thing.

You know, so fiscal partners are always -- we're always on the look-out for fiscal partners. Although, you know, we sometimes have limitations being a government agencies.

And then ultimately, to get back to the environmental justice focus, having a community focus means that you need to nurture relationships. You don't just go into a community the day before you want to do a biomonitoring study and expect people to show up. I mean, it really takes a long time. That ACE study I was talking about has been a nurtured relationship for many, many years with some of the advocacy groups in the San Francisco Bay Area.

Communication. With any scientific endeavor, communication is always a challenge. It's not essentially a worse challenge for the Biomonitoring Program, but we do have some complicated things that we're trying to distill down into not only audiences that may not have a scientific focus, but audiences that have different

cultural and other values, different -- they're coming from different backgrounds. We have, you know, just a vast number of audiences that we have to be able to communicate with.

We do some of that well. I think we can do some of it better. Again, some of it's resources, some of it's just -- it just takes some time to develop a capacity to communicate better.

Part of this is also that we have -- we have a website to maintain. We have the results return, which is whole other aspect which we've talked about it at the last November meeting. I'm not bringing this up again. But again, these are challenges to keep those things up and going and being of value and meaning -- and still be meaningful.

And finally, what I tried to do today was do something a little different, which is we had to be able to translate our -- what we do into story telling, because that's probably the primary thing that people relate to at any level. If you have a story to tell, they're more apt to listen, then if you are going in and just throwing a bunch of data at them. And we just wanted to try something a little different just to see if -- you know, what did it sound like to tell a story to get people interested in biomonitoring?

And finally, translating our results into action. Some of this is out of our control, but there is certainly still plenty within our control. For example, there is no -- there is no doubt that what happened with the history of lead in gasoline is a great story of how biomonitoring has changed policy and turned results into action.

Unfortunately, we're still dealing with lead in the environment, but at least, you know, we're able -- we understand that formula.

I think flame retardants is the more modern example of that. And you've certainly heard a lot about that today. That story is still unfolding. Obviously, as certain flame retardants go down, others go up. And does that mean that we continue -- if we continue to have policies where flame retardants are required, this is not going to go away any time soon, but yet there -- we have seen action. We have seen legislative action. We have seen political action. And that's part of translating the results.

So ultimately, the data need to be relevant, they need to be compelling, and they need to be understandable in order for action to be taken. And I think that's a challenge for us as Program and, you know, you, as the SGP, to provide guidance in that aspect, because we really

want to be able to not just produce results, but have them actually be translated into something that ultimately will result in a cleaner -- cleaning up the trash, so to speak, inside of us.

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DR. DiBARTOLOMEIS: So I stand here before you today still that little kid that wants to have a pristine river and, you know, a trash-free hike whenever I go out there. And I now know that it's not just what you see out there in the environment, it's what's also in our bodies.

So I am committed to that aspect as well. And so that same polluted stream that inspired me as a kid has now gotten me here today to try to inspire everybody in this room to think the same way, that we really have pollutants coursing through our body, just like you would see them in a stream, you know, if you were able to. And that deserves to be divulged and cleaned up.

And biomonitoring is that tool that I think does get you at that direct exposure. That's the magnifying glass that we need as detectives. The last time I stood up here, which was in November, I pondered when do I get my name up on the acknowledgement staff. And I realized, well, maybe my name doesn't go there, but certainly maybe my image.

So in honor of Dr. Seuss's birthday, which is a

couple of days ago, I think, I just wanted to remind you that I'm now in the corner kind of overseeing the forest. So thank you very much.

(Applause.)

CHAIRPERSON BRADMAN: Thank you, Dr. DiBartolomeis. You know, I think you raise a lot of important issues. And it seems like it's been awhile since we've actually discussed, you know, Program goals and the original legislation and where we are meeting those requirements, and, you know, where and how to go forward.

I would expect that there's many people on the Panel who might want to make comments. So is there anyone who wants to respond now? Just to outline the next bit. We have about 10 minutes or so for questions, and then another time for public comment, and then time for more discussion.

Dr. Quintana.

PANEL MEMBER QUINTANA: Hi. Thank you for that story. It was a nice story. I was thinking about what makes California unique, as we discussed some other times, because our Program really isn't just a smaller NHANES. It's focused on California and the concerns of Californians and the exposures of Californians.

And so I was interested in your Asian Pacific

Islander study, because that is a major population in California, and may have some cultural exposures.

But I'm just curious if you have any comments about other populations. Coming from San Diego, we have a very large immigrant community, you know, I think it's the second largest Chaldean community from Iraq, and all kinds of different populations that I'm curious if you have any comments about what makes California different or any approaches to that issue?

DR. DiBARTOLOMEIS: Well, I think we could spend a lot of time just listing what makes California so different. And I don't think that anybody would believe that if we did a CalHANES, that it would look anything like the NHANES.

We do have a large populated State with such diversity that I think is unrivaled. And we not -- on top of that, we have -- our geological makeup is quite a bit different. I mean, every state has some part of California, but California seems to have a lot of them -- a lot of those things.

So just the fact that we're so big and so diverse makes the challenges much more difficult. But I think in terms of approaching, there are many different ways you can do this. You can approach it based on, let's say, a chemical of concern. Let's just use pesticides for an

example.

If you wanted to look at a community that might be higher -- more exposed to pesticide issues, you go to where the pesticides are used and then you nurture that community and you do some kind of a study there, and we have examples of how that's been done.

The issue in the San Francisco Bay Area and other places where fishing is sometimes used for not just sporting, but for subsistence, you start getting into, well, higher levels of chemicals will be going into their bodies because of the contaminated fish. So that's maybe more of a cultural reason to go in and look. You know, the chemicals are of concern. You know the communities there, but are we -- is it because this group is different because they're actually fishing for living, not just fishing for fun or something along those lines.

You might be approached by a community. We think we are more greatly -- higher impact because we live by these facilities that are spewing these things out or there's a waste site near by. That's another way that we might get involved.

Now, each State has their own pockets of that, but we haven't really -- we haven't really done anything in those -- along those lines as a Program. They're very resource intensive. I mean, you probably can appreciate

that. I mean, if we're approached by a community to say we live near these sites and we'd like you to biomonitor us and tell us what's in our bodies, our first thought is, yeah, that would be great, but, you know, where would we -- how would we even start?

So there's all these different approaches for bringing in that context making -- and then looking at California specific problems. And then I guess the other thing is that we do tend to push legislation and laws for the rest of the country, whether it's air or water or whatever.

And so following and tracking the efficacy of those -- of that legislation is another aspect that would make California unique in terms of biomonitoring. The flame retardant standard is just a good example of that. I don't know if I -- did I give you -- did I respond?

PANEL MEMBER QUINTANA: I was just interested in your thoughts from a Program perspective. So thank you.

DR. DiBARTOLOMEIS: Yeah, and we're -- you know, we have a continuing discussion about these things like on our -- we have meetings every two weeks, and we're always thinking about ways to draw in more -- a larger, you know, population randomness or something that would allow us to get at some of the -- answer some of these questions. Unfortunately, it always turns then back to what do we

give up?

DR. FENSTER: I just want make a very small addendum to Michael's answer, which is for the MIEEP study, I just wanted to mention that that study of pregnant women and infants did recruit primarily immigrants, Latina immigrants, and so -- and also for the BEST Study, for the Expanded BEST, we've made an effort to oversample for Hispanics, both Spanish and English speaking, and also APIs.

So we will within -- as Michael said, we will be able to within the different studies start looking at some of the issues that you asked about, in terms of cultural practices, immigration, different chemical patterns that we see in different populations and try and understand routes of exposure better through that.

DR. DiBARTOLOMEIS: That was Laura Fenster.

CHAIRPERSON BRADMAN: So I wanted to follow up on a couple things. One, definitely reiterate -- I feel less articulate today because of this cold. But I want to reiterate your mention of biomonitoring in children. That's kind of something I've mentioned many times over the years. And just because, you know, of course, children are some of the most vulnerable parts of our population in terms of both exposure and health impacts and, I think, the more information we can get on that the

better.

You know, the funding, you know, that's a much bigger discussion that we didn't go into the details today. But, you know, I think we have been, you know, a little bit successful with partnered grants like HERMOSA, where, you know, a group obtained research funding, but then collaborated with Biomonitoring California on the laboratory components, and also, you know, authorship and really substantive input about what the product of that research is.

And maybe that's something we need to encourage more. You know, I know in our group I pressure everyone to go through Biomonitoring California when we write grants. We're not doing much biomonitoring right now. But, you know, maybe that is a role that the lab can play perhaps maybe a little more aggressively in terms of additional partnerships, laboratory collaborations with other researchers, and involvement in grants. Now, we've talked about that in the past. But maybe we're at a point where we should reach out a little bit more strongly, especially with the reductions in CDC support.

DR. DiBARTOLOMEIS: Right. I mean, I would agree with you. I think that when I showed you the challenges, I think there all nested -- they're all linked because part -- for example, when you are -- even if you're just

trying to couple up with another partner, you have to be able to communicate. You know, what is it that we can offer?

It's one thing if you decide we just need to have 40 samples analyzed. So the labs might be available to do that. But if you're talking about actually study design and having it dovetail with the other types of things that we want to do, it would be nice to start from the beginning, and, you know, go after research proposals and that sort of thing. We've done that, and it is -- that's time intensive.

And I know we can continue doing that, but I don't know if they're going to be -- what my vision is is that we do a lot more of those short, you know, fast hitting HERMOSA types of things, where we're able to produce results. Have results from start to finish in a year where we actually then can go to the policymakers and say, look, here's the story, here's what happened, here's maybe some suggestions on what to do versus a five-year study, where it might -- you know, by the time you're done, maybe the people that were originally interested have left the legislature or whatever.

CHAIRPERSON BRADMAN: A little more discussion?

Dr. Kavanaugh.

PANEL MEMBER KAVANAUGH-LYNCH: I just want to

say, so one of the ways that California is also very unique is in investing State resources in research programs. And as the director of the California Breast Cancer Research Program, we have prioritized looking at the role of chemicals in breast cancer. And we would not be able to support the research that we've been able to support in that arena without the Biomonitoring Program.

It's been very mutually beneficial, and we've had many projects now that have used the Biomonitoring Program. And without its existence and its ability to respond to some of those scientific questions, we wouldn't be able to fund that research and be exploring that issue and having the success that we're having.

We have had -- we have some current RFPs out and just closed one actually looking at asking researchers to look at the role of different ways of affecting chemicals policy and evaluating their effectiveness, such as market-based campaigns, regulation, that sort of thing. We have one out now for biomarkers, which could absolutely include -- and biomarkers of exposure. So definitely very pertinent to biomonitoring as well as another RFP out on risk assessment. And so I encourage anybody who's interested in those to pay attention.

CHAIRPERSON BRADMAN: Anymore comments? Maybe I think we now have some time for public comment and maybe

it will also spark more discussion.

So thank you, Michael.

CHAIRPERSON BRADMAN: Are there any?

DR. SINGLA: Hello, it's me again. Veena Singla with the Natural Resources Defense Council. In regards to the budget for the Program, I wanted to mention that I was earlier this morning actually -- you might have seen me slipping in and out of the meeting here -- I was commenting at a Senate budget subcommittee hearing specifically on the budget for the Biomonitoring Program, and speaking to the legislature about the importance of the Program for Californian's health and tracking exposures and understanding what's in our environment and in our bodies.

And I would certainly encourage the Panel to weigh-in on this issue as well in terms of the importance of the Program with the administration in whatever way may be appropriate.

CHAIRPERSON BRADMAN: Is there anymore public comment?

Have there been any email submissions?

DR. PLUMMER: No.

CHAIRPERSON BRADMAN: Okay. Sara, it looks like you want to say something.

MS. HOOVER: Yeah. Sara Hoover, OEHHA. I would

just suggest that we page through some of Michael's slides, and you can -- as a way to structure your discussion, you can go through the different priorities that we've named. These are priorities we've presented to you previously and Michael is reiterating some of our -- you know, what we're focusing on.

So I think you could just page through and let Panel members think about this and comment on anything. I think, in general, and I actually used these same priorities to structure the talk I gave in November about topics for this year. But just like you said, it's an opportunity to again have the Panel weigh in on priorities and make any notes or comments about things we should think about as we move forward.

CHAIRPERSON BRADMAN: Thank you. I was going to suggest something similar. But just to clarify though, you're not looking for, you know, concrete recommendations or, you know, direction, rather you're looking for kind of comment and agreement, I guess.

MS. HOOVER: Well, I mean, you know, basically, the Panel is always providing input and direction to the Program. We have not posed a formal question to the Panel. There's no voting, you know, that sort of thing.

CHAIRPERSON BRADMAN: Yeah, exactly.

MS. HOOVER: So no formal recommendations, but

always input is welcome.

CHAIRPERSON BRADMAN: We're particularly quiet today.

(Laughter.)

CHAIRPERSON BRADMAN: Maybe we should go down and everyone has to say something, but -- Dr. Quintana, we'll start with you.

PANEL MEMBER QUINTANA: I'm not quiet. I guess I have a clarification question about the biomonitoring of children. Do you widen that definition to include the pregnant women or in utero exposures?

DR. DiBARTOLOMEIS: This is Michael. We haven't actually gotten into the specifics of age groups or anything. I think what we were beginning to formulate in our minds is how would we biomonitor children that are already born into this world. At the age groups that would be, you know, before they reach 16 or something along those lines. I mean, we do know that they're biomonitored for lead as part of the program, but -- I mean, not our program, but as part of the, you know, lead prevention. But, you know, to expand that, and we've heard presentations before in front of the Panel about I think from CDC and EPA about collecting specimens from children. And we just think since that is the most vulnerable of the populations more than likely for

chemicals certainly early on in exposure, we wanted to begin to go down that track.

The in utero exposures we've done pregnant -- we've looked at pregnant women. We're looking -- MAMAS samples are from pregnant. And so you could make the leap, I guess, of faith that what's in the serum of the mother could be also in the serum of the developing infant. But I don't know if we've -- you know, I don't know if we've excluded or included looking at that in more depth as to how we could expand on that population, if that's what you were kind of after.

If you're suggesting that we do go down that path, we can certainly -- it doesn't hurt to go down and see what kind of work has been done in the past that we might be able to do. But I think originally we were talking with biomonitoring, you know, like maybe from two to 16 years old or something in that age group, or maybe younger, I don't know.

CHAIRPERSON BRADMAN: Dr. Luderer.

PANEL MEMBER LUDERER: Just I think following up on that, I mean, I think -- I mean, to me, I think of this as, you know, we're at the stages of development and kind of life course idea. And so I think if you're, you know, going to be biomonitoring children, and you have been doing these wonderful collaborations with the MIEEP

program and the current MAMAS program to really try to, you know, not exclude that very early part of development, you know, prior to early childhood that you're talking about, and really including it and viewing it as a continuum.

DR. DiBARTOLOMEIS: As you were talking, I was envisioning like an optimal study that might be a proactive -- I mean, prospective study where you actually begin with a population of pregnant women, and then you -- and then as the children are born, you follow them for the first two or three years of their life or something, it sounds great.

Certainly, we can develop a theoretical project like that. Maybe it is worth pursuing and finding partners to doing something like that.

CHAIRPERSON BRADMAN: Dr. Quintana.

PANEL MEMBER QUINTANA: A follow up on the follow up. You know, that study does exist in a pilot stage, and that's the National Children's Study, and it had several sites in California. And I don't think those samples have been fully exploited, and that I was just curious about a formal collaboration with those archived samples.

DR. DiBARTOLOMEIS: Well, I think you might have known that we applied for the initial -- with UC Berkeley, we applied for one of the grants that would have set up a

center in the west coast to do the biomonitoring of all those samples and the ones that are going to be collected. We weren't successful. That doesn't mean that there wouldn't be still some opportunity possibly to hook up with the existing centers to do some of that work.

There is actually a new proposal -- a RFA out, I think. Are you familiar? It's the sort of second part of that, which is to look for cohorts. And we're exploring that also, partly as our Branch in CDPH, but it would involve some biomonitoring component more than likely.

PANEL MEMBER QUINTANA: I was thinking specifically of the archived samples from the Vanguard Centers.

DR. DiBARTOLOMEIS: Yeah, I -- that I don't even know. That's something I know something about, but I don't know how easy it would be to be able to access.

PANEL MEMBER LUDERER: There was just a notice that came out this week that the archive is now actually up and running. And so I'm sure -- I mean, I or somebody else or one of the other members, could forward that information to you, because I think that would really be worth pursuing as a program.

DR. DiBARTOLOMEIS: Yes, please do. That's new to me.

CHAIRPERSON BRADMAN: That notification literally

came out just in the last few days.

DR. DiBARTOLOMEIS: I should have been on top of it.

(Laughter.)

CHAIRPERSON BRADMAN: Dr. McKone.

PANEL MEMBER McKONE: Well, I just want -- I mean, I do want to follow on that.

CHAIRPERSON BRADMAN: That's okay.

PANEL MEMBER McKONE: I'm looking at the priorities. So I guess one of the questions is do you believe you can pursue all of these equally or are you looking for some feedback about -- the interesting thing about -- I mean, for me, looking at these, they're all really important, right, so it's hard to say, oh, this one.

MS. HOOVER: Dr. McKone, your microphone.

PANEL MEMBER McKONE: Microphone, right up next. Okay.

(Laughter.)

PANEL MEMBER McKONE: You know, they're all important. I don't know if there's ways to set priorities based on, you know, near term what's going to provide a lot of return. I look at it and go like, well, you can't throw out advanced biomonitoring science, because that's kind of like throwing out your seed corn or whatever. I

mean, you don't have anything to grow into. You just do it.

Good children we all admit is pretty important. Environment -- I think actually environmental justice and statewide surveillance might -- I mean, that could be the goal is statewide surveillance, so they might be merged a bit.

Interventions, that's a bit broad. I think, you know, like chemicals in consumer products is ripe for intervention, and we're already doing some of that. And that one might be really useful, because of its strong tie-in to a really important effort and DTSC to try and understand not only what's there, but how to get -- how to find alternatives and make sure those alternatives aren't going to be just as bad or different bad than what we have now.

So, I guess, I'm -- the question is there are some ways probably to set priorities. I don't know if you're looking for a little more detail or if you've already done this internally and have some way of ranking these?

DR. DiBARTOLOMEIS: Well, We're going to -- we're kind of thinking out loud here, right?

Yes, we have -- these priorities are evolving, and we have actually spent some time -- if you look at the

slide history since I've been here, they've been slightly different each time, not a lot, but biomonitoring children is the first time it's appeared on any of my slides. So other than if you take children out of there, we're working on all the other priorities in some capacity, manner, or form. And children you might argue that, well, we've looked at prenatal and, you know, infancy, you know, biomonitoring -- you know, we've done some work in that area.

So if you were to just kind of look at these on face value, the Program is, in some capacity, working on all of these priorities. The beauty of many of these is they can be nested and intertwined. There isn't any reason why you just follow down a path of an intervention, for example, and not necessarily think that you might include children, a consumer product, and an EJ community. I mean, you can factor all those types of things in and develop a study design that will have a lot of these elements in it.

But the truth is, as you did already point out, that you can't do everything as well all the time. You know, you have to make some choices. And so we have been making choices early in the Program. Before I came on board, there were choices to try to find surrogates for statewide surveillance or to look at targeted populations.

There was less interest or less movement at that point on doing consumer products or interventions and those sort of things. We're moving in that direction, partly because of DTSC, partly because of the -- of our emerging interests. So this is not stagnant. I think that every -- at every SGP meeting if there's a discussion about priority setting, and whatever might be -- we heard this morning about diesel biomarkers again. So there might be -- that might be on people's -- high on their list again.

So there isn't any reason why we can't continue to talk about this. But keep in mind that, you know, as we begin studies, they have to finish, and then you have to be juggling, and laboratories have only a certain amount of capacity in terms of equipment and staffing and all this sort of thing. So we don't want to get too far ahead of ourselves.

So as I'm thinking out loud, I value anything that comes -- and I know we all do value anything that would come from the expert panel on, you know, how we might try to prioritize and what is an emerging issue that has real prominence because of the timing or the times we're living in.

We didn't even put climate change up here for example. But if there are some things that would be

chemical uses that would be changing as the climate changes, you know, is that something we want to pursue?

So I -- that's all I'm going to say. I can't commit to one thing or another. But you have actually hit on probably one of the hardest jobs that I have in terms of thinking about the Program is how to identify these things, but also keep the lid on, so that we don't get too far ahead and spread too thin.

PANEL MEMBER BARTELL: Yeah. I'm going to throw out an idea here, and see what the reaction is. I look at this list, and I just -- I don't see the feasibility of statewide surveillance in the next couple of years, given the budget issues you've talked about. You would know better than I. But, you know, I understand that, you know, doing a representative sample like it's done in NHANES is an extremely expensive endeavor.

And even if it's not, you know, a complete database, still to actually take the time to do that population based multi-level sampling to try to get representation from say, for us, would be all the counties in California, and make sure we hit all the racial subgroups, and socioeconomic subgroups that we want to hit, I just -- I think -- and you again may have run some of these numbers, since you've been thinking about ideal designs, but I think that's probably like orders of

magnitude more expensive than you probably have the budget for or at least have had in the past few years.

And while I know that was sort of the original intent of the legislation, and may be great goal for some day getting to, I guess I just wonder if it's realistic in the next couple years, given what the budget is now, to even have that on the priority list.

DR. DiBARTOLOMEIS: Well, a couple of answers to that. One is it has to be on our priority list, because it's such an important mandate. It would be just not the correct thing to do to present something that is written into statute and says you shall do this. We have come up with ways to address the issue in a smaller targeted or, you know, population, or as a smaller populations were in different parts of the State.

In our optimal planning, our optimal Program design, the actual funding to do something that isn't quite the NHANES thing, but it's certainly better than what we're doing now is not totally prohibitive. Certainly with our current budget it is, but if you -- if we were to -- I mean, we haven't -- we have an exact budget that we could put forward, that puts us into, you know, probably two or three times more funds than we currently have or something along those lines. So it's not like we're talking so much money that forget it.

So it's tricky. It's a tricky thing. And again, we can couple some of our statewide surveillance ideas with children biomonitoring or, you know, you could even nest a consumer product exposure study in there, or -- and it could be -- and look at EJ issues. So it wouldn't be just statewide surveillance in a random fashion. We could do something that's a little bit more targeted, that would get at some of that randomness, as well as some of the more specific issues we've been trying to address as well. So that's -- you know, we're kind of playing that game right now.

CHAIRPERSON BRADMAN: If I were to make some comments here, I would change biomonitoring children to biomonitoring pregnant women and children. And that kind of addresses the question of prenatal exposures.

When I look at this list, to me it seems perfect, in terms of priorities. You know, but really the question that comes up is do you have the resources to do it? And I think that's kind of an ongoing challenge, and, you know, will guide the feasibility of individual pieces of this.

One question I have you just mentioned about you have an ideal budget. Is there any proposal for a budget change proposal or some other submission to try to, you know, amplify those resources to more fully fill out these

priorities?

DR. DiBARTOLOMEIS: I'm trying to figure out how to answer that without getting in trouble.

CHAIRPERSON BRADMAN: Apologies, if I shouldn't have asked the question.

DR. DiBARTOLOMEIS: We were -- I think it's fair to say that the upper management in the Department of Public Health asked for what it would take to optimize the program, and even add a little bit more, meaning that, you know, some things that are more discretionary.

You know, what would it take to make this Program function at its optimal level, laboratory-wise, as well as from the epi and, you know, toxicology side and communication and all that? So there is something written out, but it's internal. And probably the mechanism is not going to be the budget change proposal mechanism. It probably has to come through a different path. It just -- that approach is so competitive and so difficult. Given that we would have to be also identifying funding sources, it's just really a very hard thing to do.

It's better to have it be communicated as we're trying to do to various audiences and get their interest, so that they're actually asking for the information from us, and that's what we're trying to do, I think.

CHAIRPERSON BRADMAN: Can I ask, and I'm going to

drill down a little deeper, and this is -- you know, if it's not appropriate -- I mean, one thing I think about, for example, DPR has the Mill tax, and their funding is not through the General Fund.

There's work being done pesticides by biomonitoring. Is there an opportunity to collaborate with them and use some of those resources to answer questions that they might have? And are there other similar revenue streams that might kind of enhance the Program that would, you know, address pressing environmental and public health issues from different agencies in the State, but also in general serve the State?

DR. DiBARTOLOMEIS: Well, first, let me say that the Mill tax and the Department of Pesticide Regulations funds do support -- partially support the Program. There are funds coming in from that. And therefore, doing pesticide work, I think, is important to do. Going beyond kind of some basic having the panel -- you know, the pesticide panels that we do, we haven't yet approached CalEPA and DPR to see if there are funds and interest to go out and do something more, I guess, robust, for lack of a better word.

I actually don't know. Well, let's put it another way, since 2012 when I came on board, I have not

had a single discussion with Department of Pesticide Regulation about biomonitoring. That is, in part, probably my mistake, because I probably should be going there and seeing if they're interested. But it also might -- it might be a two-way street. I'm not so sure that we -- that they are wanting to put funds into something along these lines. I just don't know.

And maybe the folks at the agency at CalEPA might know better. You know, I don't know if OEHHA has any comment on something like this or not, but -- okay.

So basically, but I -- you know, you're raising an idea, and no idea is a bad idea. So I guess what I can say is it's worth me kind of scratching my head a little bit on and seeing if I can find out a little bit more.

CHAIRPERSON BRADMAN: On a related piece to something I perhaps am starting to sound repetitive, but this issue of like if we were actually to show a decline in exposures related to diesel, or I think there's been tremendous work done that we heard about today related to declines in flame retardants, and there's also been some other published literature on that.

You know, I think that when we look at the cost of those industries, in just dollar terms, and the potential public health impacts in terms of health and care and that sort of thing, we're also talking about

enormous dollars.

So I think the Program, at least the component of it, where we can generate information that show changes related to policy, and regulation, and even perhaps translating that into some sort of dollar figure or some sort of, you know, implication of the benefits, I think it can really show both the value of the Program, potentially the value of the impacts of the regulations relative to the economic costs of implementing them, and perhaps could strengthen the Program in a way that would make it more visible, and maybe it would be easier to get those extra resources.

Again, I just think the power of showing changes. You know, we started about the same time in environmental health, and everybody shows that picture of gasoline lead going down and blood lead going down in tandem. And the more that we -- not the more, but it just underscores the value of that image in really helping people understand what environmental health means, and what exposure reduction means, and how biomonitoring can inform that.

DR. DiBARTOLOMEIS: I agree.

CHAIRPERSON BRADMAN: Anymore discussion?

Well, I think on our agenda right now we have a last, and perhaps a bit longer, public comment period. Although, we've had a number of kind of -- it seems at the

end of the day, these kind of wrap together. But we have another opportunity for public comment. So we have 15 minutes for that and then we have some time for wrap-up and adjournment.

Any new public comments?

I'll repeat, are there any email submissions?

DR. PLUMMER: No.

CHAIRPERSON BRADMAN: No.

Okay. Well, at this point then, should we wrap-up?

Sara, any last comments?

MS. HOOVER: (Shakes head.)

CHAIRPERSON BRADMAN: Well, then, I think we've had a lot of good discussion today. And I just want to kind of end the meeting with a few points.

One, that a transcript of this meeting will be posted on the Biomonitoring California website when it's available. And also to let you know that the next Scientific Guidance Panel meeting is on July 28th, 2016. And that will be in Richmond at this time at the CDPH building.

So at that point, then I think --

ACTING DIRECTOR ZEISE: Let me then offer my thanks to the Panel for really robust discussions. Really appreciate your input. And you've given us a lot to think

about, especially on the diesel marker. That was something that we've been grappling with for eight years, or something like that -- since the beginning of the Program. So I thought it was very, very helpful to hear about that.

And I want to thank the audience on-line and here in the room, and, of course, our staff who is amazing and put together a wonderful set of materials to talk about, and all their good work preparing for the meeting. So thank you, everybody.

CHAIRPERSON BRADMAN: Thank you, Lauren. And I want to reiterate too, I don't think I do enough of that, really just to thank everyone in the Program who works on this. I've known many of you for years, and it's really -- it's really just astounding how much work gets done and how important it is.

So on behalf of the Panel, I want to extend that thank you as well.

ACTING DIRECTOR ZEISE: And to all the speakers. I forgot to thank the speakers in the morning.

CHAIRPERSON BRADMAN: So I guess, at this point, we're adjourned.

(Thereupon the California Environmental Contaminant Biomonitoring Program, Scientific Guidance Panel meeting adjourned at 4:04 p.m.)

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

I, JAMES F. PETERS, a Certified Shorthand Reporter of the State of California, do hereby certify:

That I am a disinterested person herein; that the foregoing California 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 17th day of March, 2016.

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