CALIFORNIA ENVIRONMENTAL CONTAMINANT BIOMONITORING PROGRAM

(BIOMONITORING CALIFORNIA)

SCIENTIFIC GUIDANCE PANEL MEETING

CONVENED VIA WEBINAR BY: OFFICE OF ENVIRONMENTAL HEALTH

HAZARD ASSESSMENT

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

STATE OF CALIFORNIA

MONDAY, MARCH 8, 2021

10:00 A.M.

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APPEARANCES

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Carl Cranor, PhD, MSL

Oliver Fiehn, PhD

Eunha Hoh, PhD, MSES

Thomas McKone, PhD

Penelope (Jenny) Quintana, PhD, MPH

Veena Singla, PhD

José R. Suárez, MD, PhD, MPH

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT:

Vince Cogliano, PhD, Deputy Director, Scientific Programs

Sara Hoover, MS, Chief, Safer Alternatives Assessment and Biomonitoring Section, Reproductive and Cancer Hazard Assessment Branch

Shoba Iyer, PhD, Staff Toxicologist, Safer Alternatives Assessment and Biomonitoring Section, Reproductive and Cancer Hazard Assessment Branch

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APPEARANCES CONTINUED

CALIFORNIA DEPARTMENT OF PUBLIC HEALTH:

Kathleen Attfield, ScD, Research Scientist III, Exposure Assessment Section, Environmental Health Investigations Branch

Jennifer Mann, PhD, Research Scientist IV, Exposure Assessment Section, Environmental Health Investigations Branch

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Nerissa Wu, PhD, Chief, Exposure Assessment Section, Environmental Health Investigations Branch

DEPARTMENT OF TOXIC SUBSTANCES CONTROL

June-Soo Park, PhD, Chief, Environmental Chemistry Laboratory

PRESENTERS:

Bill Arnold, PhD, Department of Civil, Engineering, and Geo-Engineering, University of Minnesota

John DeSesso, PhD, Principal Scientist, Exponent

Keith Hostetler, PhD, Senior Managing Toxicologist, SafeBridge Regulatory and Life Sciences Group, Trinity Consultants

Amina Salamova, PhD, Associate Scientist, O'Neill School of Public and Environmental Affairs, Indiana University

Libin Xu, PhD, Associate Professor, Department of Medicinal Chemistry, School of Pharmacy, University of Washington

ALSO PRESENT:

Nancy Buermeyer, Breast Cancer Prevention Partners

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PROCEEDINGS

MS. JARMUL: All right. It is just before ten o'clock. I am going to go ahead and introduce Vince Cogliano who is the Deputy Director for Scientific Programs of the Office of Environmental Health Hazard Assessment, OEHHA.

Vince is stepping in to give the welcome on behalf of Lauren Zeise, OEHHA's Director, who will be joining the meeting a bit later.

I'll go ahead and hand it over to you, Vince.

DR. COGLIANO: Thank you very much, Stephanie. Good morning, everybody. I'd like to welcome the Panel and audience to the meeting of the Scientific Guidance Panel for the California Environmental Contaminant Biomonitoring Program, also known as Biomonitoring California. Thank you all for participating and for sharing your expertise.

The Scientific Guidance Panel last met on November 8th, 2020. We started with an update on the biomonitoring study currently under development to evaluate the effectiveness of air filtration in reducing air pollutant exposure in an AB 617 community. Input from the Panel and audience included highlighting the importance of:

Including a control group to better interpret the

results of the intervention;

Controlling for tobacco smoke exposures and analyzing results for certain chemicals, such as polycyclic aromatic hydrocarbons;

Ensuring that we understand and are transparent about the capability of the air filtration system being evaluated, including whether it can reduce levels of SARS-CoV-2, that is the virus that causes COVID-19.

The remainder of the meeting focused on discussing challenges in biomonitoring surveillance studies informed by a series of guest speaker presentations. The main goal of the discussion was to identify surveillance priorities for Biomonitoring California. Input from Panel members included:

Highlighting the importance of tracking temporal trends in chemical exposures, while noting that this is difficult given Program resources;

Encouraging the Program to partner with biobanks and other groups to obtain already collected biospecimens for analysis, and;

Suggesting the possibility of measuring chemicals in wastewater to complement biomonitoring.

A summary of input from the November meeting, along with the complete transcript, is posted on the November SGP meeting page at biomonitoring.ca.gov.

Because we're meeting virtually today, I would like to have the SGP members introduce themselves and also your affiliation. I'll be going through the list of SGP members alphabetically. So I'm going to start with Dr. Cranor. Please unmute yourself and tell us your name and your affiliation.

PANEL MEMBER CRANOR: Hi. Carl Cranor from the University of California, Riverside. Distinguished professor of philosophy, and a faculty member in environmental toxicology.

DR. COGLIANO: Thank you.

Dr. Fiehn.

PANEL MEMBER FIEHN: I'm professor Oliver Fiehn at the UC Davis Genome Center. I'm an analytical chemist, and toxicologist.

DR. COGLIANO: Thank you.

Dr. Hoh.

PANEL MEMBER HOH: Hi. I'm Eunha Hoh. I'm a professor of environmental health in School of Public Health at San Diego State University.

DR. COGLIANO: Thank you.

Dr. McKone.

PANEL MEMBER McKONE: Hello. I'm Tom McKone, professor emeritus at the University of California, Berkeley, School of Public Health. Also a retired

affiliate at the Lawrence Berkeley National Laboratory.

DR. COGLIANO: Dr. Quintana.

PANEL MEMBER QUINTANA: Hi. I hope you can hear me.

DR. COGLIANO: Yes, we can.

PANEL MEMBER QUINTANA: I'm a professor of public health at San Diego State University.

DR. COGLIANO: Thank you.

Dr. Singla.

PANEL MEMBER SINGLA: Hello. Good morning. Veena Singla, Senior Scientist with the Natural Resources Defense Council in the Healthy People Thriving Communities Program.

DR. COGLIANO: Thank you.

Dr. Suárez.

PANEL MEMBER SUÁREZ: I'm José Suárez, associate professor in the School of Public Health at the University of California, San Diego.

DR. COGLIANO: Thank you.

And our Chair, Dr. Schwarzman.

CHAIRPERSON SCHWARZMAN: Good morning. Thanks, Vince. I'm Meg Schwarzman. I'm in the Environmental Health Sciences Division at the School of Public Health at UC Berkeley. And if we've had all of the Panel members introduced themselves?

DR. COGLIANO: Yes, we have. So now it's time for me to hand it off to you to Chair the meeting. Thank you very much.

CHAIRPERSON SCHWARZMAN: Great. Thanks so much, Vince. Right here at the outset, I just have an ex parte contact to disclose. In September, 2020 I was contacted by phone by Mr. Greg Hurner of Carpenter Sievers -- Sievers, sorry -- Carpenter Sievers, requesting a meeting to discuss evidence on quaternary ammonium compounds, the subject of today's meeting, which we will refer to as QACs. And I just directed him to submit materials or comments through the Program staff.

So I want to review the goals of the meeting for the Panel today. In the morning session, we will, as usual, receive a Program update. And we'll then review possible options for statewide surveillance, which was what we discussed at the November 2020 SGP meeting. And staff has since developed further ideas based on that discussion, so we'll review it today.

The remainder of the meeting will focus on the SGP's consideration of quaternary ammonium compounds, or QACs, as potential priority chemicals. To inform our deliberations, we'll hear from four guest speakers, Bill Arnold of the University of Minnesota, Amina Salamova of Indiana University, Libin Xu of the University of

Washington, and Keith Hostetler of Toxicology and Regula -- Toxicology Regulatory Services.

As usual, there will be time for questions from both the Panel and the audience after each guest talk.

After the presentations, the Panel will formally deliberate on whether to recommend QACs as priority chemicals for the Program for Biomonitoring California. And that session will include three parts, an overview of the potential priority chemical document by OEHHA, a public comment period, and then a discussion by Panel members.

And the final option of the day, after the deliberation and discussion by the Panel members, is an open public comment period.

So as I mentioned, after each presentation, there will be a question-and-answer period, so speakers should remain unmuted with their webcam showing, so that they can respond to questions from the Panel and the audience.

If SGP members wish to speak or to ask a question, please just raise your hand - like physically raised your hand - and I will call on you at the appropriate time. And then at that moment, you can unmute yourself to ask your question or provide your comment. If webinar attendees have questions or comments during the periods after each talk, you have a few choices. You can

submit them via the question feature of the GoToWebinar platform or you can send an email to biomonitoring@oehha.ca.gov. That's biomonitoring@ O-E-H-H-A .ca.gov. And just a reminder to please keep your comments brief and focused on the items that are under discussion. Relevant comments will be read allowed paraphrasing, if necessary.

We can also receive oral comments from webinar attendees during the public comment periods and the afternoon discussion session. So if you wish to speak, please use the raise hand feature or the question feature in GoToWebinar, and they'll get that message to me and we'll call on you at the appropriate time.

So I would like to start our first session by introducing Nerissa Wu. Nerissa is Acting Chief of the Environmental Health Investigations Branch at the California Department of Public Health. She's overall lead for Biomonitoring California. And she will provide us an update on current Program activities and an overview of possible options for statewide surveillance.

(Thereupon a slide presentation.)

DR. WU: Good morning, everybody. I hope you can hear me.

MS. JARMUL: Yep.

DR. WU: Okay. Let me head over to my screen.

All right. Sorry for the delay. No matter how many times I do this, it takes me a minute to figure out all the different buttons.

Okay. So welcome everyone and good morning. I'm going to give a brief update on various Program activities, including the CARE Study, AB 617 work, and then where we are in consideration of our surveillance options as the Program.

But before I get to staff updates, I do want to mention that Biomonitoring California is now a member in the National Biomonitoring Network.

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DR. WU: This is an effort led by APHL to provide guidance on standardization across the state programs. We always really learn a lot in interactions with programs from other states. So looking forward to having another forum within which we can do so.

We have had some changes to staff, since our last meeting. We have two new lab people, Dinesh Adhikari at EHL, and Jagdish Dhaliwal at ECL. We've also lost one person from ECL. Ting Jiang has left her position. And we have a couple other staff changes, including Marley Zalay, who you know from this forum, who has left her position at OEHHA, and Lauren Baehner, whom you have also heard from here, particularly about metals in the ACE

Project, has left her position at EHIB. So welcome to new staff. We look forward to working with you. And big thanks to our departing staff for all of your contributions to the Program.

We have one other staff change, which is not reflected on this slide. Dr. Kathleen Attfield has taken on a new role in Biomonitoring. She will be the Chief of the Biomonitoring Investigations and Outreach Unit. So really looking forward to continued greatness from Kathleen.

CDPH staff continue to be redirected to COVID-related work, to a large extent. I think it's hard to appreciate what that means, if you're not in the Department of Public Health. But within EHIB about 80 percent of our staff have been redirected, to some extent, meaning that either some percentage of your day is spent on COVID work or you're rotating in and out of COVID positions. And then there's some people who are just working on COVID for months at a time.

So all staff are impacted. If you yourself are not redirected, you are helping cover work for your colleagues who are redirected. And this is obviously our public health priority right now and it makes sense that we're working so much on COVID. But the impacts on our Program, and on our team, and the work that we are trying

to do here, the impact is significant.

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DR. WU: So it was a year ago that we had to make the call to shutdown CARE-3 in San Diego and Orange counties. We had gone through two rounds of participant selection in accordance with our sampling quotas. But given the short period of time that field work was up and running, the breakdown of participants who were able to complete study participation did not reflect those quotas.

The next few slides are just to give you a sense of who those participants were. And we had hoped to reach 350 participants. But at the time we closed down, we had only collected samples from 90 of them.

And if you remember, we were having some delays getting our Orange County office up and running, due to difficulties finding short-term staff for those offices. And so you, if you see on this map, 84 percent of participants are from San Diego, and only 16 percent are from Orange County.

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DR. WU: Because we had to end early, the participants who completed the study did not reflect the region by race, as you see here.

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DR. WU: The majority of participants are female,

which is not unusual for a study like this. But almost all had more than a high school education, which is not reflective of the county or the region. Median age of participants is 53 years old. And 98 percent of the participants were Internet participants, meaning that they completed their informed consent, and their questionnaire, and they made their appointment online. It makes sense also, because getting the paperwork back and forth through the mail took much longer. And so in the short time our offices were open in San Diego and Orange, we didn't have time really to have that -- the paper participants get enrolled and then to give their samples.

As for how participants found out about this study, 37 percent came from a randomized household postcard, 43 percent came from Craigslist, and the remainder came from community groups, family, friends, and et cetera.

So these differences between CARE-3 and Region 3 will be important to remember and also consider when we have summary data to look at.

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DR. WU: And here's where we are with the CARE study. At our last meeting, we were on track to return results on schedule, meaning that this month we'd be sending packets out to our CARE-3 participants. But there

have been some delays in getting lab results back. The labs are also not immune to the impacts of COVID. We have been able to call back our participants with elevated metals levels in our prescribed follow-up. And we hope to have those packets -- the full results return packets out to participants soon.

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DR. WU: And then a quick update of the AB 617 projects. Since our last presentation, the team has been working to identify a facility that would be appropriate for an air filtration intervention study. So they've been focusing on schools, which will be -- we'll be looking at sites based on factors such as what are the local ambient pollutant levels, the type of filtration that they've installed, facility size, and associated economic demographic characteristics at those schools.

So we're working with Cal to identify both biomarkers and air quality -- air analytes to measure. We don't know when we'll be able to get out into the field. But the hope is that sometime by the end of the year we'll be able to complete field work.

At our next SGP meeting in July, we'll be focusing on biomarkers of effect. And so we will also feature a detailed update of the study.

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DR. WU: So what we're going to spend the rest of our time talking about is an update of where we are in our work to develop a new surveillance project. And I know we've talked about surveillance a lot. This is not to take away from intervention studies or community-focused studies. They're all valuable types of studies that were very informative. But our focus right now is trying to figure out how to continue with surveillance.

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DR. WU: And a few reminders of the context that we're working with. Statewide mandates in our legislation, and surveillance is to be used to evaluate levels of chemicals in a representative sample of Californians, to look at trends over time, and also the effectiveness of public health efforts and regulatory programs.

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DR. WU: Some of the characteristics of surveillance that we talked about last time, surveillance needs to be representative, so that we can take that data and compare it across studies and across time. We want to be collecting data that's useful, so that we can have an impact on public health. And the protocol needs to be acceptable, so that people will actually enroll in the study and take part in it. The other thing is that

surveillance really does need to be a stable protocol, something sustainable, so that we can implement it reliably across time, so that we can see temporal trends.

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DR. WU: Now, of course, the dominant factor in our discussion is always our budget and the financial realities that the Program faces. As we've discussed before, the Program essentially has the same baseline budget that we've had since 2007, when we were founded. And this budget covers only staff. There's no money in our budget for field expenses like contracts, or supplies, or rents, or participant incentives.

So one of the questions that came up in our last meeting was about how much does each study component cost and what makes sense for us to try to save on when we design a new protocol? And this is a function not just of dollars, how much does something cost in dollars, but also how the Program can spend money, so our State mechanisms for how we pay for things in the State system, the process we go through for contracting or for bringing on temporary staff. And this presents some challenges and barriers to us being able to move forward. So it's something we have to consider when we are looking at options for surveillance.

The other cost that we really don't talk about a

lot is the cost of staff time. So we have talked here about how -- the way we got CARE-LA and CARE-2 off the ground, is that our staff were working in a way that was not really sustainable. And the effort it takes to conduct any study is really considerable, but particularly something like CARE, where we're moving from region to region. So every time you go to a new region, you've got to scout out the region and understand it, make connections with stakeholders, conduct outreach, find venues for sample collection, and then you have to find staff to run your offices.

So, at the same time, your staff is also doing things like developing quotas, selecting participants, and then managing those participants through the system. So this is really resource intensive in terms of staff hours. And so if you have a protocol that takes a lot of staff hours, those staff can't be doing things like analyzing statistics and getting data out of the Program. And that has been a challenge for the Program. It's something that we have really struggled with.

Somebody recently asked me what would it take for us to get back into the field doing CARE the way we were, one region at a time. Just a rough estimate I came up with was that we'd really have to almost double our budget, in order to get back to doing a sustainable CARE

program. So that just gives you a little bit of a context of our budget.

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DR. WU: So the last time we talked about some of the factors that we would want to consider and we heard about this in the overview in the introduction. Some of the things that I heard in our discussion were that the time trend is a priority. We want to really be able to look at exposure over time.

While we might not be able to cover the entire state, it might be important to compare sectors, like rural versus urban might be important. We heard that we should focus on things that make California unique, the border area, immigrant population, pesticide usage, air pollution. We also heard that we should look for less expensive ways to biomonitor, for example, using samples that are already collected, or to evaluate exposure through wastewater surveillance.

Well, today, I want to provide you an update of where we are in our consideration of these options. With the input that we got, we have narrowed this down to a few possible types of studies, either obtaining samples from an existing study or working with a program with good coverage of the state. So that could be a health care provider, or some other blood collection program like

Genetic Disease, or we continue to do field work the way we have been doing it, but really limit the geographic region that we're trying to cover.

And at this point, we are still talking about our conventional biomonitoring with blood and urine samples. We did note that there was interest in looking at wastewater surveillance. It's something that we would like to continue to learn about and consider maybe as a companion to biomonitoring or as a way to screen for emerging chemicals at some point.

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DR. WU: So just in brief, we did look at studies that might have banked samples. These are just some examples of those. All really excellent studies, but not really designed to reflect an underlying population. So in that way -- not really a good match for surveillance.

The other issue was that they are generally not ongoing into the future. So if we're looking at exposure in the present or in the future, these are not examples of sources of samples that might work out, but always willing to hear about other studies. If you have other ideas of studies we could look into, please let us know.

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DR. WU: So we'll be focusing on the other three alternatives from the last slide. And the scenarios I'm

going to describe to you, this is very high level. These are just potential study designs. This is still very much a work in product -- progress. Just a report back on what our current thinking is.

So the two big costs of studies that we've talked about are participant management and field work. So with that in mind, we've really focused on study designs that minimize those expenses.

So the first example is partnering with a high coverage health care provider. And with this, we could design a study that would cover the state, or a region, or a really limited focused area depending on the provider's coverage, and then we could select participants from the membership rolls in accordance with our eligibility criteria.

And then we have talked about the potential of partnering with Kaiser, as we did for Project BEST. Kaiser has the broadest coverage across California. And we have experience with working with them. And when we conducted BEST in 2013, this was the first collaboration of its type. And there were a lot of issues to work out. It was a very resource-intensive study. And this is not something we could support at this point in our Program.

But there have been many studies since then. Kaiser's research arm has really evolved since then. And

we've started to have some discussions with staff about how this might work out. And it's been sufficiently promising and that we do want to continue to learn about how this might work.

So one of the benefits of working with Kaiser is that they have the ability to order lab work. The samples of research are part of their medical request menu. So your participants could just go to the Kaiser lab that they normally go to, and the protocol for collecting that sample would already be in the system as a standard operating procedure.

The flip side of that is that the protocols are established, so the Program would have no ability to change that protocol. So that's an element of control we would lose. Also for Kaiser collaborations, Kaiser staff really are the initial point of contact for participants. So that whole task of participant interface also takes place outside of the Program in a little bit of loss of control over that.

The benefits of this kind of collaboration are really clear. It's a sampling frame for which we have the contact information, the potential participants are already in a relationship with Kaiser, and there's a potential to look at exposure data along with health outcome data, which would be great. And there's no need

to set up a field office.

However, in some ways, it's a huge advantage for our staff to not be charged with participant outreach and enrollment. But again, it is a little bit external to the program, so there would be some loss of control over how a study is conducted.

And, you know, when we talk about surveillance into the future, being able to collect this data for years into the future, this would require an ongoing partnership with Kaiser or whichever health care provider we work with. And again, that is something that would not be totally within the control of the Program.

We do need to figure out what costs would look like. Presumably, we'd have to pay for some Kaiser time, staff time, and, of course, sample costs. So we're continuing to look into this to figure out how it compares with the cost of doing our own study and whether it's something that the Program could afford.

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DR. WU: Another option that we're considering is the high coverage sample collection program like a Genetic Disease Screening Program, GDSP. This is something we piloted in MAMAS, but this gives us an opportunity to do something a little different, in that we could do random selection, and again, define that geographic area, whether

we want it to be statewide, or regional, or in a smaller focused area as a breadth versus depth argument.

But we could work with GDSP to get demographic information. And in early talks with GDSP, we have indication that we would be able to get, if not exact addresses, we could get some blurred geocodes for where participants are coming from, and we'll have to think about what that means in terms of identifying things like drinking water source or air quality.

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DR. WU: Considerable benefits of this protocol. We would have the ability to do probabilistic sampling over whatever geographic area we chose. In this case, there would be no concern about participant rates or participant enrollment or management to worry about, no field office.

Another unique benefit of this type of study is that the cost of samples is lower than when you have actual participants signing up, but it's also a transaction within the State, which is easier for us to work with, than contracting with outside vendors or hiring staff externally.

The Biobank does have samples from the past. And so, it would be possible, for example, to do a PFAS temporal trend looking back in time, and then moving

forward as we collect samples into the future.

The samples can also be used as a screen for emerging chemicals, which is interesting. We do know about some of the downsides of these samples. It's only serum. There is a contamination issue, so that we wouldn't be able to measure -- there are a number of chemicals we wouldn't be able to measure. And we have talked about how this is a subset of pregnant women in California, those who enroll in the State Prenatal Screening Program. And then there is no exposure information or interaction with the participants themselves.

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DR. WU: Finally, we've talked about a model, in which we would conduct participant recruitment and field work, much like we've done in the past for studies, but we'd really limit the scope to a particular geographic area. I think last time, I mentioned Sacramento County is maybe an area where we could do urban, rural, or maybe some agricultural areas. Although, based on cost, doing something in our immediate vicinity of our office, like in the Bay Area, would make sense logistically.

The model could accommodate probabilistic sampling, or we could continue quota sampling, as we've done for CARE.

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DR. WU: Adapting CARE to something that focuses on narrower -- a narrow geographic area close to our office does reduce the cost of field work, but it doesn't eliminate it. So we'd still have to figure out a way to cover those costs. And if we were to conduct probability sampling, we could look at temporal trends for that focused area, but it would not give us an estimate for statewide exposure.

Another challenge is that in order to do probabilistic sampling, we would need to get a sampling frame that file of contact information for eligible individuals in our area. And this is actually a considerable expense and requires a lot of staff time to manage.

There is participant selection and recruitment also. Studies like NHANES spends enormous effort on this component of the study. Sixty percent of NHANES participants require six contacts before they sign up. So this would be a lot of participant management on the part of our staff.

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DR. WU: So you can see how these potential studies compare. There are benefits of each type, but there are also challenges of each type. So our continuing

task is to further develop these protocols, get some more information about the cost, so we can really hone in on this list. We anticipate that we will not be out in the field conducting surveillance work in the next fiscal year.

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DR. WU: But our hope is that by next summer, we'll at least have a direction, so that we can start developing a study protocol. And as always, we welcome your input and advice on this.

So with that, I will end my talk and open it up to questions.

CHAIRPERSON SCHWARZMAN: Thank you so much, Nerissa. We have ten minutes here for questions from the panelists. And just a reminder of how we'll proceed. The panelists can restart their video and then just raise your hand. And I will keep an eye out and call on you.

So we'll start with Veena.

PANEL MEMBER SINGLA: Thank you so much, Nerissa, for that very informative presentation. My question was about the GDSP and would there be the ability to return results to participants through that program?

DR. WU: No. Whenever you get samples from GDSP, you do not have participant IDs. There is linkage that can happen, so that they can get us information. You

could -- there are studies that link vital stats, for example, in newborn outcome data. So that is a possibility, but we don't actually get the participant identification. So there is no interaction directly with the source of the sample to the participant.

CHAIRPERSON SCHWARZMAN: Taking off on that point - thank you for that Veena - you know, I know that's a hallmark of the Biomonitoring Program under this -- or the studies under this Program. How have you thought through approaching that of not being able to do results return in that setting?

DR. WU: Well, so results return is one of the things that -- one of the real predicates of the Program and it's also part of our values is right-to-know. So being able to return results and have a conversation about the significance of the results, I think it's really part of building community capacity and understanding of environmental health. So it's hard to give that up.

However, we could do broader kind of education and outreach not of a particular population. These are not your samples, but, you know, we could still reach out to mothers, or pregnant women, or to a general audience of, you know, this is what we're finding in the pregnant population.

I should say that the results return effort is

not insignificant, and so there are benefits of not returning results, right? You know, that frees our staff up to do other things. The other thing is one of -- one of the issues we've had with doing non-targeted screening is it creates some issues with results return. And so having anonymous samples actually would free us up to do some of that work.

But, you know, it is a mixed -- I do have mixed feelings about it, because I do feel very strongly that having this interaction and having this educational component of our studies is really important.

CHAIRPERSON SCHWARZMAN: Thank you for those thoughts, Nerissa. It was really helpful.

And I -- one of the things I'm hearing you say is some of the options that it actually opens, like doing non-targeted screening and undercurrent constraints, you know, sort of maximizing staff time, while recognizing that it's not the goal of the Program, but it does accomplish -- it does -- it potentially helps accomplish some other goals under very -- a setting of constrained -- resource constraints. So anyway, I appreciate that sort of elaboration.

Other questions from panelists?

Yeah, Oliver.

PANEL MEMBER FIEHN: So one of the problems in

collection -- collections is, of course, you know, having a person go into a doctor's office or somebody who's collecting the blood. There are alternatives, like dried blood spots and dried plate spots, which would be sent by mail and then could be sent back. Is that a possibility that has been considered, or is that just so little material, or so contaminated that it would be of no use to the Program?

DR. WU: Well, sure, I mean, I think it would be great to have different media that are more -- that are easier to collect. I think there is a question about the contamination. I think Jessica Nelson in our last forum from Minnesota was talking about it, and they've recently put out data on how the dried blood spots they were collecting in their newborn program really had very poor correlation with the cord blood for a mercury study they were doing. And we want to look at that carefully and think about whether the blood spots really are a good representation of exposure.

There is, of course, the potential for contamination. Even in a hospital setting, you have -- the blood spots are in all sorts of environments. But if they're coming from people's home, you don't have a whole lot of control over how that blood spot is taken. These are the concerns with urine samples, where you want to be

really careful about how they're handled, and managed, and sent back to you.

So I think it would be interesting to look into -- and actually I'd like to hear from our lab folks about what the method might look like and whether there'd be enough material for them to really do a lot of screening on those samples.

CHAIRPERSON SCHWARZMAN: Any other panel members?

Yes, José, please.

PANEL MEMBER SUÁREZ: I have a question about CARE-3. So is the thought right now then to not resume CARE-3 down the line?

DR. WU: I do not think we will be resuming CARE-3. When we first shutdown, when we thought it was not a long-term shutdown, there was a thought that maybe we would be able to pick up where we were. At this point, we would have to start completely over again, because we're, you know, a year out. We'd have to restart an office, restart with participant -- with new participants. We just do not have the funding for that right now.

PANEL MEMBER SUÁREZ: (Nods head.)

CHAIRPERSON SCHWARZMAN: Eunha, did you have your hand up? Yeah.

PANEL MEMBER HOH: Just curiosity that I want to hear Nerissa's opinion thoughts about. If, you know,

multiple different studies or the ways to recruit the participants, I think there it seems like obviously some sample amounts, you know, the volume is limited, so the one participant, you know, subject we cannot measure every, you know, the priority chemicals from the one subject. It maybe has to be -- like these participants have to be measured for this and these different participants have to be measured for different chemicals. Do you have any thoughts on that, or is that a limitation, or do you think it's okay?

DR. WU: Sorry. If I understand your question, correctly, you're asking for the Genetic Disease samples, if we don't have enough volume, could we just get like two pools of samples and do different analytes on them? Yeah, I mean --

PANEL MEMBER HOH: Right. Yeah. Yeah.

DR. WU: And that is one of the things about doing probabilistic sampling that you are creating a generalizable set of data. So, yeah, that would be possible, if we had the funding to purchase two sets of samples. I think the limits are if we wanted to do POPs -- if POPs were a priority of ours and we really wanted to do lipids, that is a possibility that we could have a set of samples set aside for that. But because it's serum and because there is this contamination issue,

there are some analytes that we just won't be able to do even if we have the volume, metals in particular. And, obviously, all the urine metabolites we won't be able to do.

PANEL MEMBER HOH: Um-hmm.

CHAIRPERSON SCHWARZMAN: Veena.

PANEL MEMBER SINGLA: Two questions. One is a topic I know we've discussed numerous times on this Panel, which is related to the NHANES program. But I thought I would just ask again, given there's, you know, a new administration, and just wondered if it's -- if there's any opportunity to potentially partner with what NHANES is doing in California or leverage any of their samples at all. It's -- like I said, I know we talked about this before and there's a lot of challenges there, but just thought I'd -- I'd ask given new federal context.

And my second question is about the potential utility of other kinds of biological samples, like hair, teeth, and nails, and might there be any role for those -- those kinds of samples that tend to be a lot easier to collect?

DR. WU: For the first question, I'll say that NHANES data for California, it is not a recent issue that it's difficult to get NHANES data for California. That's something that has -- that has -- that has been an issue

for many administrations. So I don't think the new administration will have a -- will have bearing on that. Though, Jennifer, who has -- Jennifer, chime in if you have anything else to say about NHANES.

As far as other media, hair, nails, and teeth, I think they do suffer from some of the deposition issues, like how representative they are, like where in your hair do you take that sample, for example? So I think those methods are worth pursuing. I don't think it's the Program's role necessarily to do that methods development. But certainly, once those methods are robust and demonstrated would be something that we'd be interested in looking at.

DR. MANN: I'll -- I chime in about the NHANES question. Can you hear me?

DR. WU: Yeah. Thanks, Jennifer.

DR. MANN: So NHANES is not designed to be representative of any state, so we can start there. They always include California. They usually include LA County -- somewhere in LA County. But those samples are meant to be used nationally, so they're not representative of LA County either. They do a lot of their Hispanic sampling in LA, and things like that. So that's one of the issues.

The other is NHANES is notoriously private about

where they're doing their samples, even though now I imagine an Internet site that will identify each county where they're doing the sample in the country, because people can see the trailers.

But those are two issues that have gone back since the beginning of NHANES. So they really have to do with their sample design and their high level of confidentiality.

MS. HOOVER: Hello, Meg. This is Sara. I just want to make sure everyone knew that was Jennifer Mann. Just remember --

DR. MANN: Sorry.

MS. HOOVER: -- everyone who speaks to identify themselves and hopefully share your webcam, if you're commenting.

I actually wanted to chime in in response to the hair/teeth question from Veena. We actually examined different media early in the Program and there are a number of issues with hair. There's contamination issues. We actually settled squarely on blood and urine. And urine is pretty easy to collect in fact, at least that's been our experience overall. So I don't think that that would be a positive development or a feasible path. As Nerissa said though, we'll definitely keep our eyes on, you know, innovative methods development and keep that in

mind.

CHAIRPERSON SCHWARZMAN: Kathleen, did you have something?

DR. ATTFIELD: Yeah. Hi. This is Kathleen Attfield from CDPH. I just wanted to chime in on the -- another aspect of the NHANES question and that we've recently had the biomon -- the CDC biomonitoring meeting across granted states, which doesn't include us now, but because everything is virtual, many other states are able to participate. And they really put a big focus on the difficulties, the complexities, and the expense of all the field work and sort of the very epi heavy side of surveillance that many states are now trying to do. A lot of states have started off with more community or local based sampling, and now many more are trying to do more representative statewide sampling.

So they, in that meeting, had really recognized that a greater coordination and maybe cost sharing of resources at the -- you know, across states and nationally was something they wanted to look into. And that could really benefit us down the line, because there is a bit of every state starting from scratch. And so that's more resource and cost intensive of course.

So thanks for the question.

CHAIRPERSON SCHWARZMAN: One final brief question

before we move on to public comment. Forgive me, Nerissa, if you already explained this in your presentation and I missed it, but, you know, I know that Kaiser covers about a quarter of the State's population, but I imagine it's not truly representative. But are there sufficient numbers to get a truly representative sample of participants from Kaiser's membership?

DR. WU: I actually am going to call on Jennifer Mann again for this, because she has looked into the comparison between Kaiser's population and the underlying population.

Jennifer.

DR. MANN: Yes. This is Jennifer. And now I'm sharing my webcam. So, yeah, they actually --

MS. JARMUL: Sorry, Jennifer, we can't hear you very clearly.

DR. MANN: Because my headset --

MS. JARMUL: There you go.

DR. MANN: -- my microphone was not in the right place. Sorry about that.

So Kaiser has -- has done -- routinely does comparisons with the demographics of their population and the demographics of California, plus other insured populations. So they have a lot of underlying data that would allow us to do a probability sample and then weight

it properly to be reflective of the population and they have plenty of members. The one thing that I'm not sure about is what the coverage is in different parts of California. So I imagine in the northeastern parts of California, there may be less coverage, so that's one area. But in the most populated areas of California, it has good coverage and is pretty reflective of the population. But as I said, that's not a deal-breaker, because they have all the information they need to do proper weighting.

CHAIRPERSON SCHWARZMAN: Great. Thank you for that, Jennifer.

I want to -- let's see, José has one final question. You know what let's do, I want to move -- can you hold on to that José, because I want to make sure we get public comment in. And if we have remaining time, let's return to that.

So we have about 15 minutes allocated, a little bit less now, for public comment. And I will just turn first to Elizabeth Marder to find out if any comments have been received.

DR. MARDER: We do not have any comments yet, but we do have one hand raised in the audience.

CHAIRPERSON SCHWARZMAN: Why don't we call on that person for the comment.

DR. MARDER: Okay. That is Jianwen She. I'm unmuting you now.

You will need to unmute yourself as well.

There you go.

DR. SHE: Yes, I did.

And can you hear me?

DR. MARDER: We can.

DR. SHE: Yes. Jianwen She, Biochemistry -- Section Chief of Biochemistry.

I'd like to address and answer Professor Fiehn's question about the dry blood spots. So generally consider like contamination might be a problem. We did some dry blood spots work with 50 microliters, that's equal to one blood spots. We did PCB, PBDE analysis. From this process, we learned contamination issue can be very well avoided or overcome. For examples, you can measure the metabolite, which environmentally may not have the capability to convert the parent compound into the metabolite. That's one way.

Secondly, like PCB, you know that 209 line congeners, environment have the dominated PCB. We call it indicator PCB. But in human bodies tended to be the coplanar PCB, which might not have like 77, 126, 169 line. It's more -- maybe more important for Biomonitoring Program is coplanar PCB. There are a lot of -- except the

77, 126, 169 line is rarely found in the contaminations. So now I can see a lot of examples, 2 through 78 is most toxic dioxins, 17 of them out of 210. So biomonitoring the relevant for the Biomonitoring Program congeners, you also can address contamination issues.

Third approach, Nerissa already mentioned like Minnesota, basically you try to team up with genetic disease program try to convince them to use the device, in this case is a filled paper -- filter paper to collect dry blood spots. You can pre-wash, pre-clean up the filter paper, which can be mutually compatible between the two programs.

Some laboratory already start on that. I forgot that's GE, which holder, the manufacturer workman, they already started the cleanup of filter paper. We collaborate with them also. So that's I'm sure try to overcome the challenge. It might be worthwhile and then I believe laboratory can get it done.

Thank you.

CHAIRPERSON SCHWARZMAN: Thanks very much.

So just a note to panelists that we do have following this public comment period, we still have 20 minutes for Panel discussion and recommendations to the Program about surveillance screening.

So keep noting your thoughts. And I just want to

check with Elizabeth if we have any more public comments?

DR. MARDER: We do have an additional -- we have no comments or emails, but we do have an additional speaker -- person who would like to speak, if I may, unmute them.

CHAIRPERSON SCHWARZMAN: Great.

DR. MARDER: Nancy Buermeyer. I have -- I am unmuting you. And you will need to unmute yourself and you should be free to speak.

MS. BUERMEYER: How does that work? Can you guys hear me?

DR. MARDER: Yes.

MS. BUERMEYER: Excellent. Hi, everybody. Nancy Buermeyer with the Breast Cancer Prevention Partners. I'm sorry not to see you all in person. I always love coming to the meetings when able.

This may have been a more appropriate comment for the end of the day, but I'm not sure what my schedule has in store for me. So I just wanted to let everyone know, first of all, how much we love the Program, which I am frequently saying to all of you. But I'm also continuing to try to get more funding for the Program. And Nancy Skinner, who is the Senator for the area of the State where the Program lives, is now the Chair of the Budget Committee. So our focus right now is to try to urge

Nancy -- Senator Skinner to make this a priority funding -- a priority Program for her to fund.

And I think it would be super helpful if this body were to send a letter to her talking about the need for additional funding. And just FYI, the request that I have put in right now is for two million a year going forward from general funds.

So fingers crossed, we're continuing to organize more folks in support, and I just wanted to let folks know that I'm working on that.

DR. WU: Thank you.

CHAIRPERSON SCHWARZMAN: Thank you for the update, Nancy. In the past, the Panel has coordinated at times on a letter, you know, that's obviously separate from the Program itself, to the heads of each of the organizations that oversee the Program. And then we've left it up to individual Panel members, if they wish to, you know, use that letter to advocate with their elected officials or anything, but I'm happy to hear other discussion if there's additional activities that people would like to take.

Sorry, I just muted myself.

Elizabeth, if there's -- I just want to check for any more raised hands, because we are still in the public comment period.

DR. MARDER: No raised hands. No comments. No questions.

CHAIRPERSON SCHWARZMAN: Okay. In that case, thank you for those. And we can return to Panel discussion and recommendations, any input that we have for the Program, about the additional work that they have done in the interim about options for statewide surveillance following up on some of the discussions that we had at our last meeting, and directions that you would like to see the Program go, or other ideas for -- they could investigate.

And I want to start with José who had a question or a comment right before we went to public comment.

PANEL MEMBER SUÁREZ: Very good. Thank you.

So just following up on some of the surveillance options that Nerissa was mentioning, it kind of seems like the combination of Kaiser with the focused area surveillance may be some of the best sources of participants to reduce the costs and to maintain how representative the sample is, at least from the Kaiser side, yes, I guess we don't exactly know how much it's going to cost per participant or sample ultimately collected. But I could imagine it would be a lot less than having to run the study by itself.

I think Kaiser is just present in most parts of

the state. And for some of those areas of which there is not that great of coverage, then that could be then switched over to focus areas surveillance, so then we're kind of focusing on specific groups of concern. It could be a thought. I like the thought process that you have been going through and looking at the different options maybe for this.

DR. WU: Sorry, to clarify. If I understand you, you're recommending Kaiser in areas where their -- where their coverage is robust, and then in areas that are not well covered by Kaiser, we would do our own probabilistic surveillance in those areas?

PANEL MEMBER SUÁREZ: Yeah. Well, to the extent possible, because that is complex in itself, because there are --

DR. WU: Right.

PANEL MEMBER SUÁREZ: -- going to be a lot of areas. And even if you are trying to recruit a small number of participants in some of the outlying areas of the state, that's still going to require a good amount of effort to do that. But I would say kind of reduce the scope of the focused area surveillance and maybe target certain areas in which you're trying to include participants of certain characteristics that would be underrepresented.

DR. WU: Um-hmm. Thank you.

CHAIRPERSON SCHWARZMAN: Jenny.

PANEL MEMBER QUINTANA: Hi. Can you hear me?

CHAIRPERSON SCHWARZMAN: (Nods head.)

PANEL MEMBER QUINTANA: Can you hear me?

DR. WU: Um-hmm.

CHAIRPERSON SCHWARZMAN: Yes, we can.

PANEL MEMBER QUINTANA: Okay. Great. Sorry, I'm having some audio problems here.

I guess of your options, I like the focused area surveillance the best, because given that we don't have a sudden influx of new resources, which, of course, would open up more possibilities. But I feel like it's better to do a focused area well using quota sampling, if necessary, to be reflective of the area than to try and do the whole state, which is, you know, bigger than many countries. So I guess for what it's worth, I feel like the focused area sampling, we have a chance at least to get a good snapshot of that focused area. And I think it's probably, given the limitations we've seen of the CARE studies, like the beginning of CARE San Diego, where we skew educated, skew white, skew older, I'm not sure that would be any worse than data that's not representative for other reasons. So I guess I would vote for the focused surveillance, perhaps using Kaiser or not.

And then again just continuing to explore existing samples. You've listed some there. I know there's probably others, but again to get away from extremely high cost of doing your own epidemiology, and your own sampling, and your own transport of the samples, and et cetera.

Thank you.

DR. WU: I think something you said made me think about another point I wanted to make, which is that, you know, in this fairly lean time of the Program, I also want to think about types of surveillance that might be modular, that we could start small and build onto. So, for example, if we start with one focused area, if the Program does grow eventually, then we can add on to that and maybe have several focused areas or, you know, to start growing our area of coverage.

I would -- you know, CARE actually started that way as well thinking that we'll start with one per year and eventually we could grow to two or three regions per year, which didn't happen, so -- for whatever reason, I'm still optimistic that we will grow at some point, but I do like the thought of being -- like thinking ahead to these -- how this might fit into a series of building blocks to a point where we have statewide coverage.

CHAIRPERSON SCHWARZMAN: Go ahead, Jennifer.

DR. MANN: Yeah. I don't know if you can hear me. I am unmuted. Am I -- okay. So I just wanted --

CHAIRPERSON SCHWARZMAN: It's quiet.

DR. WU: Where is your mic.

DR. MANN: Same issue. Okay. So my comment is that I really want to emphasize the importance of taking a probability sample approach over quota sampling. The main issue is that with quota sampling, we have no idea even if the demographics we know about are reflective of the underlying population, if everything is under -- is reflective of the underlying population. So that's where a probability sample is really important.

And at the National Biomonitoring meeting that just took place, this is the approach that states are taking now and that they're really encouraging. So I just want to make a plea for doing probability sampling over quota sampling.

CHAIRPERSON SCHWARZMAN: Jenny, go ahead.

PANEL MEMBER QUINTANA: Hi. I do acknowledge that probability sampling is the best way to extrapolate the data. One other point I forgot to add is that if we can't -- if we need to narrow the scope -- to perhaps narrow the scope in age, so that we're not trying to interpret, you know, body burden of lots of different ages at the same time. So perhaps focus on young adults, for

example, and try to -- try to limit our sampling of -- become a narrower age band in order to kind of increase our capacity to make predictions, at least about that age group, and look for trends, as an idea.

CHAIRPERSON SCHWARZMAN: I wanted to pick up on an element that was in Nerissa's presentation, which was about just in reflecting the input that we gave at the November meeting, where several of us, I think, emphasized the need for constructing studies, so that you can make comparisons over time. And I know that I was one of those people. And partly, it reflects my research where I'm really trying to look at how things change over time. And it's so difficult, because there are so few data sources that collect data that's consistent enough, or the populations are consistent, or the methodology is consistent, the, you know, analytes measured are consistent, that we can make any of those comparisons.

And I know there's lots of good uses of data that are snapshots in time, but I think there's a real need for the ability to make comparisons over time. You know, I think I mentioned in our last meeting that the research that I've been involved with for the last few years, we're able to see the impact of -- for example, just looking in the area of phthalate exposure, we're able to see some phthalate concentrations decreasing in the population at

the same time as others are increasing. And it corresponds to when some category was listed by Prop 65 -- you know, several phthalates were listed Prop 65, and then other phthalates kind of came into use as substitutes.

Excuse me.

And we can't see that without, you know, comparable data over time, and that's using NHANEs data. So that's data that's consistently collected over time. And I totally get that there are -- that it's a resource limitation issue right now. But I guess I just wanted to raise that point again that if there are ways in doing like what Nerissa is talking about of sort of a modular program that could be scaled up, if there's a way to really keep in the forefront the notion of collecting data that will be comparable in the future, even as, you know, you're not able to sample the whole state, and so there will be areas that are not sampled that you have no way of making comparisons with.

And some of that is just unavoidable, but keeping the need for making time comparisons or the value of making time comparisons in the forefront, as you design the more limited versions of studies that could be expanded with time and budget.

José.

PANEL MEMBER SUÁREZ: Yeah, I completely agree

with you, Megan, about being able to compare trends over time. That's kind of one -- some of the more important pieces that we're concerned about, right? So are these exposures getting worse or getting better for the ones that we're most concerned about?

Just kind of touching base -- touching back on some of the core issues, right, which is the budget ultimately. Have there -- have any of you done any analyses about if you want to pursue going down the Kaiser Permanente line, even though we still don't know what the cost may be, how much -- how far can we stretch the budget ultimately to -- with the current restrictions that there are, if we were to do something focused or is it possible for you to be able to do something more probability sampling using Kaiser throughout the whole state. It's really a consideration in the end of budget, right? So you can still use Kaiser, but maybe there's not enough budget to include a large range of people, and then we can proceed saying something like Jenny was proposing, just focus a little bit more within something that's still a probability sampling within Kaiser, or something like that. Have you gotten to do any of those budget considerations of what could be feasibly done with the budget?

DR. WU: The short answer is no. That's kind of

our next step as we dig one layer down to try to think about feasibility. One thing I have thought about is -- one of the issues we struggle with in state is that our funding is fairly inflexible, fiscal year bound, and there are only certain ways you can spend it. So that is a challenge with a group like Kaiser, where we have to have contracts and it's a long-term process between deciding you're going to do a study and having participants actually on the line.

One of the advantages to something like Genetic Disease is that it's flexible. You don't have actual people on the hook that you're talking to. And so if we suddenly got money, we could say, let's go buy samples. With a study, once you get out in the field, you can't stop. You need to know ahead of time that you're going to have this funding and have no uncertainty about whether you'll be able to follow through into collection of samples and all that.

So I haven't done a comparison of how much each of these cost and whether they're feasible yet. Like I said, that's kind of our next steps. But I am thinking about the kind of mechanism of how we get this stuff done. And one of the things that strikes me is that the Kaiser model might be much more difficult than a model where we're just buying samples essentially from Genetic

Disease. So that's just another thing to consider.

PANEL MEMBER SUÁREZ: Well, just a -- just a quick thought too. I mean, there's a lot of COVID surveillance happening. Have you thought about finding ways in which to link up to some of those screening methods as to be able to do some of the same things, since they're collecting samples?

DR. WU: That is a good point. Actually, Genetic Disease is doing some COVID work, I believe, using their samples -- kind of going the other way using their samples with COVID surveillance. But, yes, that's a good thought and something which we've actually started to reach out a little bit within the Department and see what other kinds of surveillance programs might be amenable to working with us.

It is a little bit of a hard time to start asking the research questions of COVID, because everyone is so focused on just getting a handle on COVID. But as things get under control a little better, I think that is a worthwhile direction to explore.

CHAIRPERSON SCHWARZMAN: Veena. Sorry, I didn't see your hand.

PANEL MEMBER SINGLA: Thank you. Building a bit off of José's comment, I do think it would be really useful to kind of see a comparison of what each of these

approaches can get the Program kind of within the confines of the current budget. And from my perspective, each one the proposed approaches has its -- has it's own pros and cons, but they're -- it's worth sort of continuing down the road to look at each of them and then kind of look at that comparison of what's the -- what's the impact, you know, that you can -- you can get within the current budget.

And -- and what -- what might it look like to have, you know, maybe a hybrid model, I think like a -- like what some other Panel members commented on. Like, if you did Kaiser and some of -- some GDSP, or -- you know, versus just one approach 100 percent.

So I think that that kind of comparison would be very helpful.

DR. WU: I agree. I also -- I think it's a good exercise for us to go to -- go through, just in case, I mean, there are extramural sources, or if our budget does expand, we do want to be ready and have some models in place, and have thought through that question.

So we are continuing -- I mean, our intention is to continue with these three types of studies and continue to kind of cost them out in more of a general -- generalized way and continue kind of honing down the list, but also get a little more specificity in this table that

I showed at the end, so that we really have a sense of what is possible.

CHAIRPERSON SCHWARZMAN: Jenny.

PANEL MEMBER QUINTANA: Hi. I just wanted a quick follow-up question. You said you started to explore what other routine surveillance is going on. And I think that would be very useful to perhaps have more information, at least from my point of view, for like how many blood samples are collected and tested for lead in children, for example, in the state, STD sampling. I'm just thinking out loud of different sampling and surveillance that's done. It might be kind of interesting to see the whole suite of surveillance and kind of look at that as a whole, and if it's possible to partner. And I thought about blood lead specifically, because, you know, it's collected in a fairly contaminant-free tube compared to some other -- some other blood tubes.

Thank you.

CHAIRPERSON SCHWARZMAN: Any other thoughts or input you want to provide?

Yes, Oliver.

PANEL MEMBER FIEHN: Yeah. I was encouraged by the comments that I've heard about the dried blood spots, it was less negative than maybe we thought. So I would encourage the Program to look more into it, based on those

comments. Maybe do a small trial or at least review the literature, talk to experts. That might be good.

DR. WU: Noted. Thanks.

CHAIRPERSON SCHWARZMAN: Kathleen, did you have something to add?

DR. ATTFIELD: I just wanted to add the comment that while we're talking about surveillance at this moment in time, that, of course, this doesn't encompass the entirety of what we're learning from biomonitoring in California. So I really take Jenny's point and working with other programs, of course, that are already also collecting some biomonitoring types of data, but also our lab collaborations, and the studies that they work with, and how that reveals information about patterns in California. So, you know, that also will get folded into our surveillance work in understanding what is happening in California.

CHAIRPERSON SCHWARZMAN: José.

PANEL MEMBER SUÁREZ: I don't know if this is the right moment to ask or not, although it's kind of related to the funding piece. Is it now possible for more direct collaborations - I'm really talking about subcontracts ultimately between researchers and the Program - to be able just to fund some of the personnel time and just the cost of keeping the labs running, given that, you know,

there's a lot of research happening and a lot of investigators may be interested in running and measuring a lot of the different compounds in some of their own studies? Is that a possibility at this point?

DR. WU: Yeah. I know Jianwen is listening and hopefully June-Soo as well and can chime in on this. Both labs are engaged in collaborations with external researchers. And they are asked often to provide services analyzing samples. And that can be anywhere from like really a broad collaboration where we are more involved with the actual sampling of interpretation or a lab fee for service. So both labs I think are quite involved with that.

It is -- I mean, there are, I think, limits to how much that can support the Program. One of the challenges is that, you know, some of the analytes that researchers are looking for we cannot always guarantee a timeline turnaround and whether we'll have staff or equipment in place to do those analyses. I'm thinking of the phthalate methodology. We don't have an analyst now and the machine is being used for something else. The lab suffers also from a lot of underfunding. And, I'm sorry, I sound like a broken record, because I always say this, but they don't have the ability to have things like preventative maintenance and duplication of instruments,

so if one goes down another one can be used. And we don't have -- we don't have cross-training, so you have multiple staff who can run a particular analysis.

So it's not a private lab. That's not how we run. And so it can be difficult for us to make those long-term commitments that are needed and it's turnaround time that's needed for grant-funded research. But we do -- the labs do quite a bit of that when they can.

CHAIRPERSON SCHWARZMAN: We have time for just one more question, comment, piece of input for the Program before we move on to the topic of QACs for the rest of the day. So if you have any final thoughts about surveillance testing and things that you'd like the Department to think about, now is the moment, excepting, of course, that you can always send ideas to the Program and they like receiving those.

DR. WU: We do.

CHAIRPERSON SCHWARZMAN: Okay. If there's no more input from the panel, Nerissa, I want to thank you for this update and thank you to the Program also for running with, you know, the notions, including incorporating some of the ideas that we discussed at the November meeting. And it's really nice to see the continued evolution of the Program's thinking on this. So thank you for that and we'll move on to the next part of

the program.

DR. WU: All right. Thanks, everyone.

CHAIRPERSON SCHWARZMAN: I want to introduce Shoba Iyer. She's the staff toxicologist -- or a staff toxicologist in the Safer Alternatives Assessment and Biomonitoring Section at OEHHA. And she's going to introduce our main topic for today, which is the consideration of the class of quaternary ammonium compounds, QACs, as potential priority chemicals.

So I'll turn it over to you, Shoba.

(Thereupon a slide presentation.)

DR. IYER: Okay. Great. Let's see, can you confirm for me that you can see my presentation in full-screen mode?

DR. MARDER: Yes.

CHAIRPERSON SCHWARZMAN: Yes.

DR. IYER: Okay. Great. Thank you very much. Good morning, everyone. So in my presentation this morning, I'll provide an introduction on quaternary ammonium compounds being considered today by the SGP as potential priority chemicals. This is the first of multiple agenda items in today's meeting on this class of compounds.

Later in the afternoon, I'll deliver a presentation highlighting some of the content that is

covered in more detail in OEHHA's potential priority chemical document.

--o0o--

DR. IYER: Here are the past SGP actions on quaternary ammonium compounds, or QACs. In March of 2019, the Panel requested a preliminary screening of this class. In July of 2019, the Panel reviewed OEHHA's preliminary screening and recommended that we prepare a potential designated chemical document on QACs. In early March 2020, the Panel considered QACs as potential designated chemicals and recommended that the class of QACs be added to the list of designated chemicals. And at that same meeting, the Panel requested that OEHHA prepare a potential priority chemical document on QACs.

We've provided a PDF of this document to the Panel members and we posted a PDF of it on the Biomonitoring California website on the page for today's meeting. OEHHA's previous two documents on QACs are also posted on this meeting page.

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DR. IYER: The SGP can recommend priority chemicals for biomonitoring in California from the list of designated chemicals. The criteria for recommending priority chemicals are the degree of potential exposure, the likelihood of a chemical being a carcinogen or

toxicant, the limits of laboratory detection, and other criteria that the Panel may agree to.

Note, that these criteria are not joined by the term "and", and the Panel is not required to specify other criteria.

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DR. IYER: The general chemical structure of QACs includes the cation NR4+. These compounds contain a nitrogen atom with four covalent bonds. The R groups are often, but not always an alkyl chain or benzyl ring.

These are the chemical structures of three QAC subclasses: benzylalkyldimethyl ammonium compounds, or BACs; dialkyldimethyl ammonium compounds, or DADMACs; and alkyltrimethyl ammonium compounds, or ATMACs. And here are examples of QACs in each subclass: Benzylhexadecyldimethyl ammonium chloride is an example of a BAC; didecyldimethyl ammonium chloride is an example of a DADMAC; and hexadecyltrimethyl ammonium chloride is an example of an ATMAC. The alkyl chain length for these compounds is typically between eight and 22 carbons long.

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DR. IYER: Now, here are the chemicals structures of selected QACs that do not belong to any of the three subclasses I just reviewed. There are a number of polymers with quaternary ammonium centers, called

polyquaternium compounds. Shown here is an example polyquaternium 42. Esterquats are another subclass of QACs in which the alkyl chains contain ester linkages. Cetylpyridinium chloride is an example of a QAC containing a pyridinium ring. And the herbicides diquat dibromide and paraquat dichloride or other types of QACs.

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DR. IYER: QACs are used in a variety of applications, including as antimicrobials, preservatives, antistatic agents, softening agents, surfactants, and corrosion inhibitors. The class we're discussing today includes all types of QACs.

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DR. IYER: I'm showing you here a picture collage of a variety of products and applications that QACs are used in. I talked about this topic more extensively in my preliminary screening presentation to the Panel at the SGP meeting in July of 2019.

QACs are used in some cleaning products, like disinfecting surface wipes and sprays. They're used in some antibacterial hand soaps, hair conditioners, other personal care products, like hair care items, facial cleanser, and body wash, lotions and mouth wash.

They're used in some cosmetics. They're used in fabric conditioners or fabric softeners. They're used in

some eye drops, topical antiseptics, and oral antiseptics, some clothing or textiles, and shoes. They're used in some swimming pool algaecides, and used in oil and gas operations, which includes hydraulic fracturing.

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DR. IYER: After our guest speakers' presentations and my afternoon presentation, the Panel will have an opportunity to deliberate on QACs as potential priority chemicals.

At that time, the options for the Panel will be to: recommend the class quaternary ammonium compounds, or QACs, be added to the list of priority chemicals; defer consideration of QACs; or decide against adding QACs as priority chemicals.

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DR. IYER: This concludes my introductory presentation. I'm happy to take questions at this time.

CHAIRPERSON SCHWARZMAN: So we have time now for clarifying questions before our next presentation. And they can come from either the Panel or from the audience.

Panel members, you can just raise your hand and audience members will alert the organizers who will alert me. Let's start with Tom.

PANEL MEMBER McKONE: Sorry. I had to find the unmute button. So you were showing all these different

types. And, I mean, you showed slides with the main compounds we considered, and then you showed alternatives, which are related, and then you also discussed several uses. I just want to get a little clarity about when we talk about the class of quaternary ammonium compounds, how wide of a net will we be covering or is that something we have to decide? If we're just going to say anything that someone would classify as a QAC is in the class or is it only going to be like the ones on the first slide that are truly, you -- know, have the central nitrogen structure and the common variations used primarily in disinfection products?

DR. IYER: We're considering the whole class of QACs. This is what the Panel voted to recommend adding to the designated list and that's the class that we're considering as potential priority -- or discussing as potential priority chemicals today.

So I will point you to the preliminary screening document OEHHA produced in 2019 and the potential designated chemicals document OEHHA produced last year for some of the chemical structures and descriptions that describe the variety of the class.

CHAIRPERSON SCHWARZMAN: Eunha.

PANEL MEMBER HOH: So the QACs that are we continuously finding new sources or do -- at this point,

do we know the -- pretty much know what are -- the main sources are?

DR. IYER: My sense is that we're continuing to find new sources. And I say this because one of the new pieces of information that's been released in the last year is information that the Government of Canada has produced. They were doing a collection of information on what QACs are used in their commerce. And the list -- the information they have now shared includes 800 QACs. And so for your reference when I was initially looking up, you know, how many QACs can I find in this class, I located about a hundred, so there -- they've received information on many more. So I would say that we're still learning a lot.

CHAIRPERSON SCHWARZMAN: Oliver, did you have your hand up? Yes.

PANEL MEMBER FIEHN: So you said, you know, because all QACs are -- all QACs are concerned, and QACs are characterized by having tertiary ammonium cations, how do you like restrict it to things that are industrial used and industrial produced and not endogenous compounds like choline, carnitine, and so on, which are obviously, well, compounds that we have in our diet?

DR. IYER: Yeah. I think -- I think that gets into more of a laboratory method discussion. And I don't

know enough to know what would be captured in a single lab method. I'm not sure if there -- there's another input you want to add in, Sara.

MS. HOOVER: Yeah. I was just going to chime in and say, yeah. Basically, Shoba, I was going to say a similar thing. So the idea, Oliver, is we typically -- nowadays, as you may recall, we tend to look at entire classes. Now, remember, there's no obligation that we monitor everything in a class. It's just the opportunity to choose whichever member of the class we wish to biomonitor. So any decisions about what's actually measured would obviously take those issues into account.

PANEL MEMBER FIEHN: Okay.

MS. HOOVER: Now, I will add that one of the topics that came up, when you all voted for the entire class to be listed as designated chemicals, was the option to potentially restrict it to a narrower set of chemicals. Ultimately, you decided against that. The Panel voted unanimously to include the entire class and asked us to bring back the entire class, but I just wanted to remind you of that discussion.

CHAIRPERSON SCHWARZMAN: Thanks Sara. Elizabeth, are there questions from the audience?

DR. MARDER: There are no questions and no raised hands at this time.

CHAIRPERSON SCHWARZMAN: Okay. Other clarifying questions from the Panel?

I guess one thing that I -- that was a little bit on my mind that's not quite a clarifying question, but just to raise from -- based off of what Sara just mentioned is one of the things that I think the Program has been responding to in moving toward naming -- designating chemical classes is the notion of sort of serial substitution, and also the variety of uses, and that certain categories -- certain subgroups of a class of chemicals are used in some applications and subgroups are used in other applications, and that that -- in the past, as we've deliberated, designations around potentially large and vary inclusive classes like PFAS, that has been what's kind of raised to the fore is that it -- rather than endorsing that the Department -- or that the Program should monitor for so many members of a large class, that it gives them the flexibility to select the most relevant chemicals to monitor, potentially as industrial uses shift or as new applications are encountered, and that kind of thing. So just sort of to pick up on what Sara said, that was something that was on my mind.

Any other questions for Shoba before we move on to the next presentation?

Oliver.

PANEL MEMBER FIEHN: Well, you know, not knowing what the next presentations will tell us, do we have reasons to -- or other newer reports that focus on one or the other class of quaternary ammonium compounds with respect to accumulation, toxicity, and so on concerns? Is there any thing that we -- that we will hear -- I mean, I don't know what we will hear, right? But, you know, something that may be is known to the Program but not yet detailed or so? If you understand what I'm trying to say here.

DR. IYER: You know, I think I'll point you to the potential priority and potential designated chemical documents we put together. And I think I'll ask you to sit tight, and, you know, we'll learn some information and have more opportunity for a discussion on, I think, this point later today.

PANEL MEMBER FIEHN: Okay.

CHAIRPERSON SCHWARZMAN: Thanks, Shoba.

Elizabeth, if there's any other questions from the audience we should tend to, and if not, we'll move on to our next presentation.

DR. MARDER: There are still not, at this time.

CHAIRPERSON SCHWARZMAN: Okay. Thanks so much for that. Thank you, Shoba.

Let's move on to our next presentation. I want

to introduce Bill Arnold who is a professor at the University of Minnesota in the Department of Civil, Environmental, and Geo-Engineering. His research focuses on the fate of organic chemical pollutants, including industrial chemicals, pharmaceuticals, and pesticides in natural and engineered aquatic systems. And he'll present on environmental detection and degradation processes of QACs.

(Thereupon a slide presentation.)

DR. ARNOLD: Thank you, Megan. I seem to have trouble sharing my screen at the moment. I have the little button.

DR. MARDER: We saw it.

DR. ARNOLD: Oh, wait.

CHAIRPERSON SCHWARZMAN: That's good.

DR. ARNOLD: Okay. Got it. It was sharing. I didn't notice it.

So thank you. I'm Bill Arnold. I'm at the University of Minnesota in the Department of Civil, Environmental, and Geo-Engineering. It is winter, so we have some snow on the ground unlike this funny picture here. And I'm going to apologize up front. I'm going to have to -- I have another commitment after the lunch break, so I won't return for those discussions. So if you have any questions about my talk, be sure to ask them when

I'm done presenting here.

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DR. ARNOLD: So the work I'm gong to present was not done by me. It was done by two of the researchers in my lab: my post-doc -- former post-doc, Sarah Pati, who did all of the environmental detection work and method development there; my former PhD student Priya Hora, who did all of the experiments looking at the fate and degradation of the compounds under environmental conditions. Annika Heaps was an undergraduate in our lab. And all of our mass spectrometry work was done in the University of Minnesota Masonic Cancer Center facility.

And the funding for this work came from the Minnesota Environmental and Natural Resources Trust Fund, which is how State lottery dollars are spent and invested in the State of Minnesota.

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DR. ARNOLD: So as Shoba explained, there are a large number of quaternary ammonium compounds. And she talked about the benzalkonium compounds, the dialkyldimethyl ammonium compounds, and the alkyltrimethyl ammonium compounds, which are in various consumer products and other materials.

There are also another set of compounds that we were interested in looking at and these are the ionic

liquids. And you'll see these have somewhat different structures in the quaternary ammonium groups. Sometimes this compound is in the ring. And these molecules have been proposed as green solvents as alternatives to volatile organic solvents like toluene, or hexane, or the like for use in chemical synthesis.

There are also a wide variety of other compounds. So domiphen is another disinfectant. This pyridinium compound with the C16 chain on it is actually in various mouthwashes. And our work with the QACs started in 2017 and 2018. And we were interested in finding out what was present in wastewater and in the environment, and for some of the reasons I'll describe later.

But then when the pandemic hit, we realized that a lot of the compounds in the list N approved disinfectants from the U.S. EPA for looking at coronaviruses or for disinfecting coronaviruses contained quaternary ammonium compounds. This little pie chart shows that over half of the disinfectants recommended contain either benzalkonium chloride, or dialkyldimethyl ammonium chlorides, or a combination thereof. So usage during the pandemic has almost certainly increased.

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DR. ARNOLD: So there are various routes of these compounds to the environment, so the ionic liquids are

more likely to come from industrial settings if they're being used as these green solvents. Of course, it could also be used as cleaning agents in commercial buildings and the like as well.

And then antiseptics and disinfectants might be more household type of usage. In our work, we did not look at the potential sources coming from agriculture. So the diquat and paraquat herbicides. Although there may be some of these compounds used as surfactants or dispersants in agricultural settings. Once we get into the environment, there are various processes that can occur. These compounds are hydrolytically stable and they're non-volatile, so those properties aren't going to degrade quaternary ammonium compounds. But there was a previous review that suggested that removal by sorption to the sediments, biodegradation, and photolysis or reaction mediated by sunlight would be the major degradation processes in the environment.

And so we wanted to not only look at samples from potential inputs into the environment, specifically wastewater effluents and then where they might wind up in the environment, which is the sediments, but also look at these degradation products to get an idea of the persistence of the QACs in aquatic systems.

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DR. ARNOLD: So just to give a quick overview of our workflow. We either took sediment samples or collected wastewater samples, and I'll give you the locations where we got those later. We do some extracts the QACs out of that matrix. And then we use a high-resolution liquid-chromatography mass spectrometry system where the chromatography separates all the analytes and the mass spectrometry allows us to detect individual analytes that we have standards for and even some that we don't.

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DR. ARNOLD: So for the wastewater effluents, we collected about a liter of water. And these were composited usually over a 24-hour period from the wastewater treatment plant. And we needed about 250 ml of this -- or milliliters of this and we would add some surrogates in there with isotopic labels, so we'd be able to evaluate our extraction efficiencies through the process.

We would extract this with a specific cartridge that does weak cation exchange to take molecules that have a positive charge on them. They stick to the matrix. We would then elute that with a formic acid acetonitrile mixture, evaporate off all that solvent, and re-dissolve it in acetonitrile and some internal standards to assess

the performance of the chromatography.

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DR. ARNOLD: So our method is a little unusual, in the fact that it is a normal phase chromatography method, meaning that more hydrophobic and larger molecules come out first and smaller molecules come out later in the analytical run. And this -- we did this, so we could see those ionic liquids, which are much more hydrophilic and much smaller and wouldn't be retained in a reverse phase chromatography scenario where the hydrophobic compounds are retained much longer.

We're actually trying to develop a reverse phase method as well, based on actually some of Amina's work that she'll talk about later, because it turns out that there are some advantages to having both operating. But essentially what this means is that when we inject our compounds into the system, the initial solvent going through the chromatograph is the organic solvent, so it's mostly acetonitrile. And over time, we take the gradient and make it more and more hydrophilic and add in water into the system with an ammonium acetate buffer and formic acid.

And then as the compounds are eluted off, they're detected by the mass spectrometer. And because we're using a high resolution mass spectrometer, it look at a

wide range of masses with very high resolution to allow us to detect a whole bunch of different compounds.

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DR. ARNOLD: So overall, the workflow is some -- what I've described here is this extraction and then analysis, but the data on the back end is non-trivial. So if we're doing target screening, we have standards of the compounds we're interested in, and we calibrate the instrument to look for those. And so we can look at relative recoveries. We can subtract for blanks, because we know what those compounds are. And blanks you do have to subtract for, because these compounds are everywhere. And then we can get the actual concentrations in field samples.

The other thing we're able to do, because we're using this high resolution mass spectrometer, is something cause suspect screening, where we can look for masses that are indicative of compounds that we don't have standards for. So let's say we have a benzalkonium chloride where we don't have the standard for a specific carbon chain length, but we know the fragmentation and parent ion mass. We can tell the mass spectrometer to look for those ions. And if we find those and the retention time makes sense, we get something called a suspect.

And we do some calibration and blank subtraction.

If they are based on what we see in our blanks, we use the software to look for potential compounds. And then based on those suspect candidates and the calibration curves for other compounds that were in our target screening, we can get an estimated concentration of what's in these samples.

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DR. ARNOLD: So just to give you an overview of what we found in the wastewater effluents, these are the DADMACs. So the limit of quantification for these is rel -- is on the higher end of our spectrum for our compounds, so between 50 and 130 nanograms per liter, depending on which compound we're looking at. The recoveries by the extraction method are relatively low. They tend to be about 15 to 20 percent. So -- but we did see between 200 and 1,500 nanograms per liter and most of these compounds were above the limit of quantification.

For the benzalkonium chloride, our limits of detection are much lower, 2 to 14 nanograms per liter. The recoveries were better than for the DADMACs. And the concentrations were, you know, somewhat lower than the tens to hundreds of nanograms per liter with a couple of them reaching into the micrograms per liter level. And again, in basically, two-thirds -- three-quarters to 90 percent of the samples that we saw the benzalkonium chlorides.

And then the ATMACs, again, we have lower detection limits here, but much lower levels of detection overall, only in the tens of nanograms per liter in the wastewater effluents.

Now, one other compound that we found, because we were screening for all these ionic liquids was this specific one here. And note this is not the C16 pyridinium compound that's used in mouthwashes. This is a C4 pyridinium compound. And the ionic liquids can be isomers of the benzalkonium chlorides. So we were very careful to make sure that this is the pyridinium and it's not a small benzalkonium chloride.

We saw this in a large number of samples. And if you have an idea of where this coming -- is coming from, I would love to know it, because we have not been able to figure it out yet.

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DR. ARNOLD: So just to give you an overall view of the compounds. We see lower -- the blue squares here are recovery, so lower recoveries for the DADMACs, and higher recoveries for some of the ATMACs and the benzalkonium chlorides. And we did see domiphen as well and benzethonium, which are other quaternary ammonium compounds used in disinfectants. And, you know, between 20 and 90 percent of the time that we see values above the

limit of quantification or analytical method. And if we look at the concentrations on the right-hand graph, we can see the DADMACs had the highest mean concentration followed by the BACs and then this pyridinium compound. And most of the rest of them were less than 50 nanograms per liter in the effluents.

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DR. ARNOLD: So we know they're getting out into the environment from the effluent. The question now is how much is depositing in the sediments. So here we take a -- we don't need much sediment at all, about 250 milligrams, and we extract it in an acidified methanol, and then take that extract and dilute it into water, and then basically treat it just like one of the water samples. It goes through the same cartridge. It goes through the same extraction and the same solvent exchange, before we put it onto the mass spectrometer.

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DR. ARNOLD: Now, here we did most of our work in Minnesota, I'll show first, and then I'll show some data from California. In Minnesota, we did our work with sediment cores. And we collected these cores for a previous project looking at antibiotics. And this is three different sulfa drugs that were found in one of the sediment cores in Minnesota. So sulfamethoxazole and

sulfapyridine are used by people, and sulfamethazine I believe is used by animals.

And because the sulfa drugs were invented in about the 1930s, we don't see any of the compounds prior to 1930 or very -- well, there's some contamination from this analytical process and the sample collection. But over time, as the usage of antibiotics increases, we can see an increasing usage in the sediment cores. And we wanted to see if these same patterns would occur for the quaternary ammonium compounds, because they also came into use in the 1930-ish time range.

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DR. ARNOLD: And so this is Lake Pepin, which is South of the Minneapolis-Saint Paul area, southeast of the Twin Cities. And it's watershed encompasses about two-thirds of the state of Minnesota. And so it's a great place to get an integrated look at what's happening across the state as particles move into the lake and are deposited in sediment.

You'll notice the sediment cores go back. They can be dated using lead-210 back to the 1880s. And we see concentrations basically nothing until about 1930 when QACs were brought into commerce. And then we see concentrations rise. And interestingly enough we see a very large peak occurring about 1970 and then a decrease

over time. And then we do see, especially in the benzalkonium chlorides here, kind of constant levels post-1990ish.

So this confused us for a little while, because this did not match kind of what we expected in terms of increasing usage over time of the compounds. And whenever this happens, you tell your students go back and extract everything and do it again. And Sarah did it all again and got the same answer.

So we asked the sediment core experts and it turns out that if you look at metals in these lakes, they shows a very similar trend. And so our hypothesis here is that what we're seeing is the effect of the Clean Water Act and the upgrade of wastewater treatment plants, to secondary treatment, and industrial source controls led to lower amounts of QACs making it out of wastewater treatment plants. And then what we're seeing now, post-1990, is more of the steady state for slight increases in use over time.

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DR. ARNOLD: This is a place where we did suspect screening. So if I can go back real quickly, you'll notice we have C12, C14, and C18 benzalkonium chloride here. This peak here matched the C16 BAC, which we did not have a standard for. And so we extract out the ions

in this 91 that's in the little red box here is really indicative of benzalkonium chloride. It's the fragment of the molecule.

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DR. ARNOLD: And we can add suspect screening compounds, including the C8 and C10 DADMACs, which are used in lots of household disinfectants on the List N from the EPA, as well as the C16 BAC. And note that the pattern -- there's some uncertainty obviously in the concentration, but the pattern matches pretty much with the other BACs.

One thing I forgot to note here is this x-axis is post -- is an accumulation rate, so it's nanograms deposited per centimeter square per year. The concentrations of these sediments were tens to hun -- to about a thousand nanograms per gram, depending on the compound.

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DR. ARNOLD: So we also worked with the San Francisco Estuary Institute to take some samples. So when they were doing one of their sediment cruises, they took a suite of samples from across the San Francisco Bay Area for us to take a look at. And the lower South Bay, of course, is more heavily populated and has a lot of wastewater input, so we expected to see higher

concentrations in the more southern portion versus kind of the more river-flushed areas in the north. And these were processed just like our sediment cores, except these were just grab samples at specific locations.

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DR. ARNOLD: And like we saw in the sediment core in Minnesota, we did see roughly north to south, as you go from left to right. It's not perfect. But we do see the DADMACs and the benz -- the benzalkonium chlorides or the BACs throughout the Bay. Here, we're not able to do the accumulation rates of nanograms per centimeter squared per year, because we don't have the right kind of data about the waterbody.

But the concentrations, you know, ten to a hundred or so nanograms per gram. So they are entering San Francisco Bay.

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DR. ARNOLD: We also had a sediment core that we collected previously in San Francisco. This is from the central Bay Area. The dates here are approximate, because the St. Croix Watershed experiment station that we use here in Minnesota to do the dating of the core had trouble with the particular core. And so the -- this is their best guess to kind of the dates.

But overall, the trends largely make sense.

There are lower levels deeper in the core, where we think were back in the 1930s, and higher levels of the BACs as we move into more modern times into the '70s and the '90s. It's hard to assess whether or not there's any particular pattern, like we saw in Minnesota in terms of the effect of the Clean Water Act, but that might be much harder to pick up in a system that has tidal influences and various other processes occurring unlike Lake Pepin, which is really just impacted by humans.

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DR. ARNOLD: So the summary of our field work here is we detect QACs in wastewater effluents up to the microgram per liter range for a few of the compounds. The DADMACs and the BACs are most frequent and at the highest levels. And we also see these compounds in the sediments. And so we know they're released in the environment. They're sticking to particles. They're depositing into the water sediments. We want to know now what's happening in between and what processes might occur in the water column.

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DR. ARNOLD: So let's go back to our diagram here. And the processes we're going to investigate -- or we did investigate are photochemistry and biodegradation.

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DR. ARNOLD: So for those of you who aren't familiar with photolysis, this the process by which light breaks down chemicals, so the compound has two pathways by which it can react. The first one is known as direct photolysis. And this is where the pollutant itself absorbs sunlight. So it's absorbance spectrum has to overlap with that of sunlight that hits the surface of the earth.

The other one is indirect photolysis. And this is where something else in the water column absorbs the light. So iron, or nitrates, or dissolved organic matter. And those compounds get photo-excited and generate a whole bunch of other excited species, so hydroxyl radicals, singlet oxygen, triple excited organic matter, superoxide, hydrogen peroxide.

And this process is natural and it's very important in terms of carbon, and elemental cycling in surface waters, but also it's important for control on pollutant levels in the environment as well.

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DR. ARNOLD: So for these experiments, we want to measure rate constants of the reactions with these specific reactive species in light form. So this is a plot that shows essentially the rate of loss of the quaternary ammonium compounds versus the loss of a probe

compound for hydroxyl radicals, which is para-chlorobenzoic acid. And by comparing the rates of loss of the two compounds and knowing the rate of loss of the para-chlorobenzoic acid, we can get the rate constants of the QACs with hydroxyl radical in this case, which is generated by a combination of UV light and hydrogen peroxide in the laboratory setting.

So these reactions turn out to be essentially diffusion control with hydroxyl radicals for the ten to the tenth per molar per second, which you would initially think is great. These reactions occur very quickly, except that the hydroxyl radical concentrations in the environment are very low. So something on the order of 10 to the minus 17 moles per second.

And so like in this first order rate constant of approximately ten to the minus seven per second, and I'll convert that into other units the next slide for you.

So we did a whole suite of experiments to look for degradation processes. These compounds don't -- with a couple of exceptions, benzethonium being one, don't absorb sunlight, and so they don't react by direct photolysis. And we didn't see any reaction with hydrox -- or sorry, with singlet oxygen or triplet excited state organic matter. Really showing the hydroxyl radical is the only kind of photoreactive, photogenerated species

that was leading to degradation of the QACs in surface waters.

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DR. ARNOLD: And we proved this by looking at the degradation of some actual river water that we collected. And I'm just going to go through the upper right-hand plot here quickly and the sunlight alone is the red dia -- the red squares. And that's just in distilled water. You see very slow loss over time over nine days or so.

The blue circles labeled MRW are Mississippi River water. So these are QACs we dosed into the Mississippi River water.

And the green triangles are the same Mississippi River water, but dosed with isopropyl alcohol. And the isopropyl alcohol quenches the hydroxyl radicals. And so the fact that we don't see any reaction when that's there really shows us the hydroxyl radicals are driving this photochemical loss.

So if we take the combination of the concentration of hydroxyl radical in surface waters and the rate constant, the near-surface rate constant for photolysis is about -- the half-life is about three weeks, meaning that half the compound will be gone after three weeks, if it transmits downstream or is within this waterbody, not accounting for any other sort of loss

processes.

And, of course, that's just the near surface and as light penetration is greatly impeded as you go to depth, you integrate this over the whole depth of the waterbody, this half-life is going to become much longer.

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DR. ARNOLD: We also did biodegradation studies in river water. And here we took filtered river water just to get out the large particles, but we didn't filter-sterilize it. And we dosed in environmentally relevant concentrations, so about a hundred -- ten to a hundred nanograms per liter of the C12 versions of the BAC, the DADMACs, and the ATMACs. And then we just kind of let them stir exposed to oxygen and monitored the QAC concentrations over time using LC-MS/MS or the liquid chromatography mass spectrometry system. And we respiked these compounds three or four times over about the two-month period.

And we showed that degradation occurs over about three to seven days. And with each time we dosed the compounds, we got faster degradation suggesting there was some adaptation in the microbial community to the QACs. Now, of course, we were isolating these QACs -- sorry, these bacteria from the environment. There were no other inputs of food over time from the emission of river water.

So the QACs might have been seen as more desirable food over time, because we were putting them into the system and all the other carbon was being consumed. And we also did molecular analysis on these reactors. And we saw taxonomic shifts over time in the microbial community showing decreased richness and evenness, so a smaller number of bacteria were becoming dominant over time, but we also did not see any evidence for antibiotic resistance changes in these microcosms, which would be expected, because were well below any kind of therapeutic or toxic dose.

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DR. ARNOLD: One other piece we looked at, as part of this study, was the formation of nitrosamines from quaternary ammonium compounds. This is because we were concerned that if the QACs got into the river water and then back into the drinking water treatment plant and were exposed to disinfectants, they might make nitrosamines, which I know are of great concern in California in terms of water reuse.

And so we did this under something called uniform formation conditions, where they're exposed to chloramines for a certain period of time and there's a residual chlorine presence throughout.

We did this with analytical standards. We also

purified the analytical standards by an extra step by putting them through the solid phase extraction cartridges we use for extracting the environmental samples. And this is because we were concerned that there might be some tertiary or secondary ammonium compounds where we didn't have the quaternary compound with a permanent charge.

And those secondary and tertiary ammonium compounds shouldn't be retained by the solid phase extraction cartridge. And so those are known to be better NDMA precursors.

The -- we also used some commercial products and purified commercial products as well, to see if there was a difference between our analytical standards. And the total nitrosamine analysis looked for all nitrosamines, not just the dimethyl N-nitrosamine that's of greatest concern in Bill Mitch's lab at Stanford.

And the yields were relatively low. They're, you know, 0.003 to 0.03 percent on a mass basis, which suggests there is some potential for nitrosamine formation from these compounds, but they're likely less important than many of the other known precursors of nitrosamines.

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DR. ARNOLD: So in the last couple of minutes here, I'll just talk about where we're going next with all of this. We are -- we've been archiving QAC samples in

waste water influents and effluents for about eight months now to see what usage has been like during the pandemic. And, of course, with the pandemic and lab personnel turnover and everything, we had to archive these. And we are just now getting ready to start processing the couple hundred samples we have stored in the refrigerator.

And we are doing this both in Minnesota as well in the San Francisco Bay Area. We'll be looking at some stormwater samples for the San Francisco Estuary Institute. And another piece we'd like to do is some better spatial sampling and modeling. So actually putting in at a wastewater treatment plant, taking samples upstream near the effluent and then floating along and taking samples over time to see how quickly the QACs dissipate along a stretch of river.

Some potential issues we're interested in are effects on wastewater treatment operations. I've had discussions with some consultants where they've been concerned that issues they've been having in their activated sludge process might be affected by QACs. And there's actually a product called Quat Block you can buy to remove QACs from your wastewater to prevent this from happening. And also potential effects on anaerobic digestion, especially during elevated usage during the pandemic.

There are other questions we'd like to explore further. We wrote a little mini-review about QACs in the COVID era. And there's good data on acute aquatic toxicology, but much less data about chronic effects for aquatic toxicology. And our back-of-the-envelope calculation says that this would be a potential concern, where as like acute aquatic effects almost certainly are not.

There are some resistance issues to explore, and this is not my area of expertise. But this little diagram here is from Michael Gillings in Australia, who has shown that class 1 integrons, which is something that move or mobile genetic elements. They have a QAC resistance gene associated with them. And the fact that there is QAC resistance in the environment is not particularly surprising, because we've been using these compounds for almost a century at this point.

And again, I think there needs to be more work, given the broad number of structures about nitrosamine -- the potential for nitrosamine formation.

And one other issue we're interested in exploring as well is improved treatments. Because if we now know that these compounds are removed by settling to particles, and by sunlight, and by aerobic biodegradation processes, something like a constructed wetland, if you have the land

space, might give more time for these compound to be degraded before they're discharged into receiving waters from wastewater treatment plants.

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DR. ARNOLD: And with that, I will let things go over to questions.

CHAIRPERSON SCHWARZMAN: Great. Thank you so much for that, Bill. We have 15 minutes now for questions from both the panelists and the audience. Panelists can go ahead and just raise your hand if you have a question. And we'll start with Tom and I'll check in with Elizabeth in a few minutes about audience questions.

PANEL MEMBER McKONE: Okay. Thank you, Bill. That was a really interesting presentation. I think it gives us a lot of insight, especially about questions to ask.

I'm curious about whether you or someone else has used the kind of information that you're gathering about deposition, and transformation degradation to make some fake calculations of things such as overall persistence, or the range of transport -- you know, long-range transport potential, and, you know, if you're aware of that or if there's some ideas about who might do that.

DR. ARNOLD: We have not done that. That is on our agenda of things to do. We want to get a little more

field data to see if we can match a model to the field experiments. And we've just started -- we have a project pending with the State Of Minnesota to do this kind of work for a broad range of antimicrobial chemicals, so not just QACs, but also antibiotics.

PANEL MEMBER McKONE: Right.

DR. ARNOLD: And so we've recruited a modeler to help with that. So I see that forthcoming, but we haven't done that yet.

PANEL MEMBER McKONE: Could I follow up? I mean, it's something we'd be interested in. And I just want to suggest maybe that's, as I recall, we're dealing with, you know, hundreds of compounds. But often there's different kinds of screens toxicity but also persistence or fate, and it would help, I guess, ultimately be nice to sort these out by which ones are likely to persist along as in an aquatic system or in the environment overall.

DR. ARNOLD: Yeah. And that's going to be the -- I think, the big driving factor on that is going to be the chain length of that carbon chain, right? So the longer that carbon chain, the more likely they are to be in the sediments. I think the rate constants for photolysis are all going to be very similar. And some of those short carbon chain compounds, which may not be high-use at this point, and have different sources are likely to transport

much further.

PANEL MEMBER McKONE: Okay. Thank you.

CHAIRPERSON SCHWARZMAN: Eunha, please.

PANEL MEMBER HOH: That's very interesting work. I really enjoyed it. It's something that I was thinking like, man, these compounds are really reminding me of my work in nicotine. So much similar in terms of analysis, all the HILIC column, all this kind of stuff. And then even oxidation and photolysis making nitrosamines as well. So it's very -- different compounds but some kind of behaving possibly similar.

And I was thinking about multiple things. The -- what about the -- this compound, this QACs, like depending on pH, you know, how sensitive they are, you know, to their behaviors, depending on the pH. That's my first question.

And the second question is how much we know about the nitrosamines? You know, that I mean you showed us some work -- your work, and then is there any other studies that are finding that these compounds are transformed nitrosamines and the more air or surface, you know, non-aquatic environments.

DR. ARNOLD: Yeah. Both good questions, Eunha. The pH effects my guess are going to be -- it's going to be relatively minor, just because these are already

permanently positively charged, and most of them don't have another spot on them that's got any sort of acidic or basic functional group on them.

And so pH might affect sorption -- it certainly comes with reaction, or biodegradation. pH I think is going to be relatively unimportant, because it's not going to affect their uptake or exposure. In terms of sorption, there might be some effect depending on the if it affects the surface charge of what they're sorbing to. If the what they're absorbing to is pretty organic, I don't think it's going to matter. But if it's a mineral surface or something like that, you might see some kind of pH effect. And, you know, there are some challenges with these compounds. We don't filter our sample through glass fiber filters, for example, because the QACs just stick to the glass fiber filters.

In terms of nitrosamines, the real expert on that is Bill Mitch at Stanford. And I know he's looked at a large number of consumer products, both secondary, tertiary, and quaternary ammonium compounds, and their nitrosamine formation potential. And then one of his former post-docs is one of my former students, Tung Zung, who's now at Syracuse, and he's also done a fair amount of work with that as well.

CHAIRPERSON SCHWARZMAN: Other questions from the

Panelists at this moment?

Elizabeth, do we have anyone in the audience who wants to ask a question or make a comment?

DR. MARDER: We do. We have received a question via the GoToWebinar questions. And I can read that to you, if you'd like, and we also have an audience member with a hand raised. So I defer to you, Megan, as which way you'd like to go.

CHAIRPERSON SCHWARZMAN: Why don't you start by reading the question and we'll give Bill a chance to respond to it and then we'll go to the person with the hand raised.

DR. MARDER: Okay. Bill, I believe this is referring to something you presented on slide number 3. This is a question from David Jones. For the EPA list disinfectant pie graph, was the segment size based on number of registrations or on relative amounts of each product sold, like relative pounds or gallons.

DR. ARNOLD: Yeah, it's based on registrations. And so I just took the spreadsheet the EPA has and divided them up by which active ingredients they had. So I don't actually know how much is sold. Although, there is some trade information and it's in our little mini-review. And I think it was something like in the first three months of 2020, like more QACs were sold than all of 2019, or

something like that. So, I mean, there was massive increase in the amount used. But, yes, it could be that a lot more bleach or some other product is being used than the QACs, but I'm not sure.

CHAIRPERSON SCHWARZMAN: José, I see your hand. We had said we would unmute the participant who wanted to ask a question and then I'll go to you next.

DR. MARDER: Okay. The -- so June-Soo Park with DTSC, I've unmuted you. You'll need to unmute yourself.

DR. PARK: Hello. This is June-Soo from DTSC. Nice meeting you all. I have one question. First of all, thanks for sharing your interesting works in the presentations.

Based on your data, I'm particularly pointing out the -- your depth profile for several Q -- QACs over time. They didn't quite show anymore more increase after 1980. She -- year contrasting to the uses. You mentioned the possible reason for that was the Clean Water Act enacted. I remember the resorting in having improved the wastewater treatment system.

So you -- at the last, your future work, you mentioned you want to measure QACs before and after the pandemic. That will be super interesting to see the result. But on the other hand, you know, the -- based on your comment, we may not be seeing any dramatic innovation

due to the pandemic, if what you said was true. So -- but in contrast, we have seen some innovation changes in indoor environment and the human exposure due to the pandemic. What are -- what are your thoughts? You know, what are you expecting when you measure QACs in your sediment sample? Doesn't matter it's in Minnesota -- lakes in Minnesota or San Francisco Bay Area, you know, the -- I'd like to hear your thoughts what kind of trend will you be expecting before and after the pandemic.

Thank you.

DR. ARNOLD: Okay.

DR. PARK: It was nice meeting you.

DR. ARNOLD: Nice meeting you too. There's lots to unpack there. In terms of the indoor exposure and things like that, I'm going to leave that to the speakers after lunch, because they're going to talk about that. And then I realizing that I should have shown one more slide from Minnesota, which I don't have in this presentation. And so Lake Pepin is interesting because a lot of the wastewater that winds up there, it captures everything that's municipal, but as well as everything that's industrial, right? And so the QACs used in all sorts of industrial cleaning And various other processes as well, not just surface cleaning for disinfection.

We did another lake. It was called -- it's

called Lake Winona. And it only gets effluent from a wastewater treatment plant from a small town. And that lake, we saw basically continuous increase over time. So where it was purely municipal input, we saw increasing loads. And, you know, it's wastewater treatment plant came online about the same time, and -- but -- so there's multiple factors going there.

And in terms of the pandemic, I expect that we'll see differences in the influents and effluents that we're measuring in terms of wastewater. You know, factors of two to ten potentially, depending on how good we are analytically.

But that also depends on if the activated sludge process how well it adapted to the new levels of compounds that are in there and how efficient the sorption was. So it may be we see higher influent levels, but similar effluent levels, depending on how the wastewater treatment plants perform.

And then the sediments, my guess we're -- it will be very hard to see any sort of trends, just because sediments accumulate over time, and, you know, those slices often occupy, you know, anywhere from two, to five, to ten years, depending on what the rate of deposition is in the lake, and even spatially in a river or a -- in a river there's so much movement of the sediment, we

probably won't see any affect very quickly on the sediments. We'll have to wait ten years and look for that peak when it deposits in the lake. But that will give me the next proposal to write, so I move a little closer to retirement.

CHAIRPERSON SCHWARZMAN: So I have José and then Eunha.

PANEL MEMBER SUÁREZ: There we go. Thanks for the presentation, Bill. Very interesting. Do you have a sense of what the half-lives of these may be in the water?

DR. ARNOLD: You know, back-of-the-envelope, you know, if we take the biodegradation, you know, half-life to be about three or four days, and the photolysis one probably to be almost irrelevant in that, you know, we're talking days to weeks, depending on the light conditions and the nutrient conditions all sorts of other factors in the water. And that's the degradation processes occurring in the water column. If you have a depositional zone where they're sticking to particles, you know, you could have really rapid removal. If your river flows into a lake, my guess is you get a lot of it removed just because all the suspended particles drop out in the lake and they wind up in the sediment.

PANEL MEMBER SUÁREZ: So are they -- they're not very stable under UV radiation, right?

DR. ARNOLD: No, they are -- they are stable under UV radiation. Sorry, let me rephrase that. Under sunlight radiation they're stable. We did not try hitting them with like 254, like the UV that's used for disinfection. But those doses are so small for DNA, you usually don't get much contaminant transformation when you're using UV for disinfection. Only when we had UV and hydrogen peroxide to generate the hydroxyl radical did we get degradation. So that would be more like an advanced oxidation process, where you could get removal if you wanted to have that as a tertiary treatment step.

PANEL MEMBER SUÁREZ: Okay. Thank you.

CHAIRPERSON SCHWARZMAN: Eunha.

PANEL MEMBER HOH: Bill, just -- it's kind of curiosity, you know, some questions. You know, I really liked your study that you also had targeted analytes and then you had the suspect screening put together. You might have already talked about it, but how many, like what percentage of the analytes that you targeted in advance and then you sort of like added more, you know, later?

DR. ARNOLD: Yeah. Our initial target list I think was 26 compounds.

PANEL MEMBER HOH: Um-hmm.

DR. ARNOLD: And then our suspect list was, I

think, another 25-ish or so, of which we saw about 12.

PANEL MEMBER HOH: I see.

DR. ARNOLD: And some of those we've now added to our target list. So the C16 BAC, the C8, and the C10 DADMAC.

PANEL MEMBER HOH: Um-hmm.

DR. ARNOLD: And then there's a couple of ethyl -- there's the benzalkonium chlorides with an ethyl group on them -- on the ring.

PANEL MEMBER HOH: Um-hmm.

DR. ARNOLD: And those are used in a lot of compounds. And so it turns out standards for those are really hard to find. So we actually bought some products and we're going to run the act -- you know, extract the actual products, just so we can figure out where the peaks are, so we can look for those.

PANEL MEMBER HOH: I see. Great.

CHAIRPERSON SCHWARZMAN: Tom, go ahead.

PANEL MEMBER McKONE: Yeah. One more quick question. I know we're going to break soon. So you've been tracking movement in water systems, but is there -- are you aware or have you done any work about the relative volatility? I mean, what's the air-water partition? Are they going to be moving in air at all or are these compounds, because of their ionization, essentially -- I

mean are they essentially waterborne transport, once they're released. I mean, that's where they're released. Is that where they go or do they volatilize at all?

DR. ARNOLD: I think it's in the environment. If they're in the water, they're going to stay in the water. Dust might be another ball of wax, right? So they do attach to particles, so my hypothesis would be that most air transport would be related to dust. So if you're using them on surfaces outside or, I think, Amina is going to talk about indoor surfaces that dust might be the air transport, but not the chemical -- the free chemicals themselves through air transport.

PANEL MEMBER McKONE: Right. Yeah. So basically the water-to-air transport would be very, very low.

DR. ARNOLD: Yeah, the permanent charge pretty much prevents that.

PANEL MEMBER McKONE: Okay. Great. Thank you.

CHAIRPERSON SCHWARZMAN: Great. We need to break for lunch. Thank you so much, Bill, for your contributions. And I want to -- we're going to break for an hour for lunch. And before we do so, I want to introduce Kristi Morioka, who is Senior Staff Counsel of OEHHA, who will provide a reminder about the Bagley-Keene requirements for before the lunch break. And as she gets on, I just want to say that we have an hour for lunch and

everyone should please be back on the webinar no later than 1:10, so that we can start right at 1:15 as planned.

SENIOR STAFF COUNSEL MORIOKA: Hi there. This is just a reminder that this is a public meeting and so we'd like you to refrain from conversing with each other during the -- during the lunch break and discussing the items that are on the -- on the agenda for today.

CHAIRPERSON SCHWARZMAN: Thank you very much and we'll adjourn for lunch and see you back at 1:10.

(Off record: 12:16 p.m.)

(Thereupon a lunch break was taken.)

AFTERNOON SESSION

(On record: 1:15 p.m.)

CHAIRPERSON SCHWARZMAN: So I have that it's 1:15 and we will start right in with our first presentation following the lunch. Thank you all for coming back promptly.

I want to introduce Amina Salamova, who is currently an associate scientist in the O'Neill School of Public and Environmental Affairs at Indiana University, Bloomington. She holds a PhD in environmental science from Indiana University and her research focuses on understanding the effects of exposure to semi-volatile organic compounds, a group of toxic pollutants, in vulnerable populations and in the built environment. She uses state of the art analytical chemistry techniques in exposure assessment and biomonitoring. Amina will talk about increased human exposure to QACs during the COVID-19 pandemic.

(Thereupon a slide presentation.)

DR. SALAMOVA: Thank you for that introduction. Can you confirm you can hear and see my presentation?

MS. JARMUL: Yeah.

DR. SALAMOVA: Hello.

MS. JARMUL: We can hear you.

DR. SALAMOVA: Can you hear me?

I'm sorry?

MS. JARMUL: Yes, we can hear and see you.

DR. SALAMOVA: Okay. Great. Thank you.

So I'm Amina Salamova. I'm an associate scientist at Indiana University. First of all, I'd like to thank the organizers for inviting me to share my research here in this meeting.

And today, I would like to speak about increased human exposure to QACs during the COVID-19 pandemic. And really our interest in this -- in this class of chemicals was because of the pandemic. We -- we've learned a lot, I'm sure as many of you, about disinfection our indoor space, both our homes and the public spaces to keep us safe.

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DR. SALAMOVA: And, in fact, the U.S. EPA has a list, which is called List N, that has more than 400 different products listed as effective for the novel Coronavirus. And half of these products have QACs listed as ingred -- active ingredients.

So as it already was mentioned in this meeting, this was a large group of chemicals, probably including hundreds of different compounds that are used in many different applications. And in addition to being used in disinfection and cleaning products, they are used in

biocides, personal care products, medical, pharmaceutical products, and even in textiles.

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DR. SALAMOVA: So for the purposes of this talk, I will focus on three major QAC groups that have already been mentioned before, so benzylalkyldimethyl ammonium compounds or BACs, dialkyldimethyl ammonium compounds or DDACs - they're also called DADMACs, but for -- we call them DDACs - and alkyltrimethyl ammonium compounds or ATMACs. And each group has several homologues depending on the length of the alkyl chain and here I will focus on C6 and C18 BACs, and C8 to C18 DDACs and ATMACs, so a total of 19 QACs.

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DR. SALAMOVA: So when we started looking into this group of compounds, we have found out that they are mostly detected in the outdoor environment. And some of this work we've heard from Bill Arnold in the previous talk, but they've been detected in wastewater, sludge, surface water, sediments, and soils. Some toxicity data exists on some of the BACs. Most of these are animal studies. And exposure to QACs has been associated with birth defects, destruction of lipid metabolism, developmental toxicity.

And in some occupational studies, they've been

recognized as asthmagens, because they exacerbated asthma symptoms. But we were really surprised to find out that there is virtually no data on human exposure and human exposure pathways, and health effects based on epidemiological studies.

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DR. SALAMOVA: So today, we'll talk about two projects that we've done on the QAC exposures. And the first project will focus on indoor exposure. So we were interested sort of in general evaluation of assessment of the indoor exposure to QACs, especially during the pandemic, you know, considering the increased use of these chemicals. So we have chosen to use dust as an exposure assessment approach or two of the QAC exposures in the indoor environment, because dust is relatively easy to work with and to collect. And also, dust is a long-term source and sink of many semi-volatile organic compounds.

So we wanted to look at the QAC exposures in the indoor dust. But in addition to this, we also wanted to see or evaluate the effect of the pandemic on the QAC levels indoors and also evaluate the effects of using disinfecting products and disinfection practices in homes that we sampled.

So this work was published last year in ES&T Letters. And I can share the paper with whoever is

interested to get more details on this work.

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DR. SALAMOVA: So for the purposes of this study, we've collected dust samples all here in Bloomington Indiana. We were able to access dust samples collected before the pandemic from a sample archive. These samples were collected during 2018 to 2019. And we were also interested -- we were also -- we also collected samples during the pandemic with -- this was done in June 2020. We were not able to get to people's homes because of safety. And we asked people to give us dust from their vacuum bags.

From the homes that were sampled during the pandemic, we asked the residents give us information on the common disinfection products they use, and also disinfection practices, and disinfection frequency, basic information on how dis -- how they disinfect their homes. Based on this information, we identified seven commonly used disinfecting products. This included both sprays and wipes, and we analyzed them as well.

So along with this, just for purely exploratory purposes, we also wanted to look at the levels of QACs in air. This was done only in three samples. We were able to collect only three samples, because air sampling is much more difficult than dust sampling. It takes more

time. And even though it's a very small sample size, and exploratory work, I still wanted to share some of our results with you, because we think we have some interesting results.

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DR. SALAMOVA: So just briefly on the dust analysis. We sieved the dust and we ultrasonicated it with acetonitrile to extract the QACs. Our surrogate recoveries were pretty good, showing that our method efficiency was pretty good. We didn't have much of blank issues. The blank levels were less than 0.1 percent -- constituted less than 0.1 percent of the sample levels. And like I already mentioned, we analyzed for 19 QACs using liquid chromatography tandem mass spectrometry and you can find more details on the analysis in our paper I mentioned before.

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DR. SALAMOVA: So moving on to the results. You can see here the levels for the 19 QACs we've targeted shown as box plots. And this is the data for the two sample groups, the pre-pandemic and during pandemic samples kind of pooled together. The concentrations here shown as box plots. The boxes represent 25ths and 75ths percentiles, the whiskers represents 10ths and 90ths percentiles, and the black line inside the box represents

the median.

The Y axis shown as a log -- on a box scale and the X axis shows the number of carbons in the alkyl chain for each QAC shown here. So, first of all, I would like to mention that almost all QACs we've targeted were detected in each and every sample we've analyzed. So our minimum detection frequency was 95 percent.

So to our surprise, the exposure to QACs was quite widespread in the homes we sampled. The concentrations were pretty high. You can see the concentrations are on the microgram per gram level. These are considered high concentrations for the indoor environment.

And, you know, when we compared the levels with other most well known and ubiquitously found compounds like flame retardants, both brominated flame retardants and organophosphate flame retardants, the QAC levels were several times higher. They reached up to several hundred micrograms per gram in these samples.

When we look at the distributional QACs here, we can see that the most abundant QACs found in the samples were BA -- C12 and C14 BACs, C8 and C10 DDACs, and C16 ATMAC. And overall, these five compounds contributed about 80 percent to the total QAC concentrations. And total QAC concentrations here are defined as the sum of

all 19 QACs.

We know that some of these compounds are high production volume chemicals in the United States. So we think that this can probably explain some of our findings here.

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DR. SALAMOVA: So when we look at the two sample groups, so -- separately, so samples collected during the pandemic and before the pandemic, we can see that the total QAC concentrations in samples collected during the pandemic shown here, are significantly higher than in the samples collected before the pandemic. And, in fact, there is about 60 percent increase based on the median total QAC concentrations. And when we've looked at some of the individual QACs, this increase was about 90 percent.

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DR. SALAMOVA: We wanted also to look into the effect of disinfection practices in these homes. So based on the survey information from the homes sampled during the pandemic, we were able to identify different disinfections routine in homes. So in homes that reported increased disinfection routine since the outbreak of the pandemic, the total QAC concentrations were significantly higher than in homes that did not change their

disinfection practices, since the outbreak of the pandemic.

In fact, the median for the homes that was -- that have reported increased disinfections since the outbreak were about three times higher than in homes with no change.

We also looked into the differences based on how many times people disinfected their homes. So the homes that disinfected more frequently, defined here as disinfecting a few times a week, were -- the total QAC concentrations were significantly higher than in homes that disinfected less frequently, defined here as less than once a week, or did not use chemical-containing products, so they just used isopropyl alcohol. These homes also had significantly lower levels.

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DR. SALAMOVA: In fact, there was a strong linear relationship between the frequency -- how many times people disinfected their homes and the total QAC concentrations.

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DR. SALAMOVA: So now just briefly about the air concentrations. Again, I would like to point out this is exploratory work. We only have three samples here. We use these type of passive air samplers, which is called

polyurethane foam samples, or PUF samplers. There is a piece of foam sitting here underneath this dome. And the sample is deployed in the house and stays there for about four weeks and basically passively samples the air or contaminants from the surrounding air.

So to our surprise, we were able to detect QACs -- a range of QACs in all of three samples. And the most abundant chemicals found in the samples was C12 ATMAC, shown here, followed by C12 to C16 BACs, and then C14 ATMAC. So these five compounds were more frequently detected. They were detected in a lot of -- in all of -- in all of our samples in quite high concentrations. Especially for C12 ATMAC, the concentration reached up to 2,000 picogram per cubic meter.

And again, when we compare it with the more widespread and well known indoor contaminants, like flame retardants, for example, again, these levels are several times higher than for those chemicals. And the mean total QAC concentration was about 4,000 picogram per cubic meter. So we were quite surprised by these findings, because QACs are believed to be nonvolatile.

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DR. SALAMOVA: But when we look at the relationship between the log of the optimal air partition coefficient and the relationship of these partition

coefficients with the ratio of all of the QACs that we looked at in dust to the rate -- to the concentration in air, because these air samples were paired with dust samples, we see that there is almost like inverse U-shaped relationship here. And these two ATMACs that we see in our air samples fall pretty low on this curve, the -- their partition coefficients are quite low and the dust-to-air ratios are pretty low as well.

So these two compounds are pretty volatile, because they have a lower octanol air coefficient -- partition coefficients, and that's, they think, is the reason why we seed -- we see them in our air samples.

The BACs that we see kind of pull higher on the curve. And we see -- we think that the reason why we see them in our air samples is because the PUF samplers are also able to capture very fine particles from the air -- from the indoor air.

So we think that that's the reason why we see these BACs in the air samples. That's probably due to the presence of the verifying particles in the foam.

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DR. SALAMOVA: So if you remember, I also mentioned that we've also analyzed disinfection products used in the homes that were sampled during the pandemic. And when we looked at this data, we realized that there is

three products that are pretty much exclusively used in more than 80 percent of the homes. So here, I'm showing -- I'm sorry. Here, I'm showing the distribution of the three QAC groups that we looked at, their contribution to the total QAC concentrations shown here as a percentage. The -- this pattern in dust samples from both 80 percent of the homes where these products are used. And this is an average contribution for those three exclusively used products in this 80 percent of the homes and also in our three air products.

So when we look at this, when we compared the dust pattern and the products pattern, we see that the similarity is quite striking. So this suggests to us that these products could be a source of the -- these QACs in the indoor dust.

However, when we compare with the air, we can see that the pattern here is quite different. ATMACs are the major contributors to the air concentrations. And this suggests to us that air can probably have different sources of these compounds. We know that ATMACs are used in some of the air fresheners, and in some of the perfumes, and they're more volatile. So some of these products can be a source of the ATMACs in the indoor air.

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DR. SALAMOVA: So in the conclusion for this

project, our results show that the indoor exposure to QACs is quite widespread. QACs can be found in the indoor air. The QAC levels are significantly higher in dust collected during the pandemic and also higher in homes with more frequent disinfection. And we think that disinfection products can be a significant source of the QACs in house dust.

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DR. SALAMOVA: So moving on to the second project that I would like to talk about today, as an exposure scientist, I am always interested in biomonitoring of emerging contaminants. So finding this widespread exposure to QACs in the indoor environment, I was thinking, you know, if these chemicals are also found in human blood. So in order to look into this, we collected samples from the Indiana University Biobank. Again, we were interested to look at general levels of QACs in human blood. And we also wanted to see if there is effect from the pandemic on the QAC levels in blood.

So we collected two samples of -- two groups of samples similarly to dust. So blood collected before the pandemic, this was serum collected during February to August of 2019, total of 111 samples. And blood collected during the pandemic, this was done in April to August 2020, again, 111 samples. And again, participant -- here,

participants were not paired. So that these two groups of samples were not collected from the same people, because human research subject -- human subjects research was quite difficult to do during the pandemic, in terms of collection of biological samples.

But the participants in these two groups were a match based on age, gender, race, smoking status, residence, and BMI.

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DR. SALAMOVA: So again, briefly about the analysis. We extracted the blood with acetonitrile. We cleaned them up on a solid phase -- solid phase extraction columns. Our recoveries were quite good. We did have in this case some issues with our blanks. But again, in general, the blanks level did not exceed 20 percent of our sample levels. But nonetheless, we decided to be safe and we blank-corrected all of our data by subtracting the blank levels from the sample levels.

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DR. SALAMOVA: So moving on to the results. Here, I'm showing the data for the ten QACs that were detected in more than 40 percent of the samples. Again, the concentrations are shown as box plots here. When we look this data, we see that the most abundant chemicals here are C12 to C14 ATMAC - quite similar to the air

concentrations - and C12 and C14 BACs.

These four chemicals were found in about 80 to 90 percent of the blood samples, so quite high detection frequency. The levels ranged from three to six nanograms per ml.

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DR. SALAMOVA: And when we look at the two groups of samples collected before the pandemic and during the pandemic, we can see here the trends similar to what we see in dust. So there is a significant statistical difference between the total BAC, total ATMAC, and total QAC concentrations in samples between the two groups of samples with the samples collected during the pandemic being significantly higher. So if we compare the medians, the medians in the samples collected before the pandemic - this is for total QAC concentrations - is 3.5 versus 6.0 nanograms per ml. The increase of about 77 percent for the total QACs. And when we looked at some individual QACs, especially BACs, this increase was about 170 percent for some of these chemicals.

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DR. SALAMOVA: So again, we wanted to look at sort of the distribution pattern of these two QAC groups in different sample types. So here I'm comparing the distribution in blood with the distribution in dust, and

indoor air from the previous study. And we see that the -- this distribution is quite different between these three samples types. So serum is pretty much equally enriched with BACs and ATMACs. Dust is mostly enriched with BACs, but there is also some DDACs here and some ATMACs. And indoor air is pretty much enriched with ATMACs, about 80 -- 70 to 80 percent ATMACs. So we think that both dust and air probably can contribute to the levels of QACs we see here.

There is different exposure pathways to blood -- of QACs to blood, and of course, this needs more work, because we have quite limited sample size. But I thought it was quite interesting to see the differences between the distribution of the QAC groups in the samples.

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DR. SALAMOVA: So our work has limitations, like I already mentioned. Sorry.

We had a limited sample size and limited geographic coverage for our samples. Our pre- and post-pandemic dusts -- dust and blood samples were not paired, because due to the challenges of the sample collection during the pandemic. Also, in our biomonitoring work, we didn't have urine samples. And we know that some of these QACs can metabolize quite quickly in the body. However, the metabolites at this point are

not known and we were not able to measure them or collect urine samples for their measurements.

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DR. SALAMOVA: So with that, I would like to acknowledge Guomao Zheng, my post-doc, who actually did all the work, all the lab work and all the data work. So really all credit goes to him, and my collaborator, Gabriel Filippelli who helped with updating the samples collected before the pandemic and the funding sources.

Thank you all for listening and I'm happy to take any questions you may have.

CHAIRPERSON SCHWARZMAN: Thank you so much, Amina. I really appreciate that presentation. It's a concise summary of what looks like a lot of work.

We have time now, 15 minutes for questions from both the Panel and the audience. And just as a reminder, panel members with questions simply raise your hand and I will spot you. And then we'll periodically sort of -- I'll check for questions from the audience.

So Carl, please.

PANEL MEMBER CRANOR: Yes. Thank you for the very clear presentation. It does leave a question. And I understand this might be -- might or might not be beyond your pay grade. But I think one of the things that the COVID circumstances have brought about is that -- excuse

me -- individuals who do the cleaning may do that hour after hour, day after day. They may have much higher concentrations than I gather you're picking up with residues. I take it you're studying residues either residues in the air, residues in the dust. But what about the people that are gathering on the floor, or the desktops, or the sprayers spraying this material. It seems to me their concentrations might be much, much higher. Do you have any insight into that?

DR. SALAMOVA: Well, I completely agree that I think people who use these chemicals, sprayers, cleaners and other people who may use them probably are exposed to much higher levels. Our sampling was done in residential in general population of Indiana, let's say, or Bloomington. None of these people were occupationally exposed to these chemicals, as far as we know.

So we don't have any data on occupational exposure, but I think that's a very interesting angle here. And I'm sure the levels in those people would be much higher.

PANEL MEMBER CRANOR: So quick -- just a quick follow-up then. You didn't look at commercial buildings at all, I mean, where there might be multiple -- you know, you think of -- they show us pictures of airports where people are cleaning it up after every flight loads and

that sort of thing.

DR. SALAMOVA: Um-hmm.

PANEL MEMBER CRANOR: The exposures there surely are much higher. They seem like they would be.

DR. SALAMOVA: Yes. We have not looked at any of these type of buildings. So our -- again, we only sampled in the residential homes, but I am sure -- for example, one of the places where the levels would be quite high are the hospitals, or schools, or day cares. I know that in schools they disinfect very frequently, I've heard that some schools disinfect at every break. They have kids actually wipe their desks, and et cetera.

So, yeah, there are some environments where the levels would be much higher, but we have not had the chance to do sampling in those environments.

PANEL MEMBER CRANOR: Thank you.

DR. SALAMOVA: Um-hmm.

CHAIRPERSON SCHWARZMAN: So similarly, I'm kind of -- I'm interested. I don't -- I don't think this, you know, was covered by your work, but just to flag the use of, I think you mentioned, you know, in air samples, the use of sprayers. And I understand there's also foggers that are used, which is a much finer particle that's generated and tends to linger in air much longer and potentially adhere to dust, and stay airborne, and

therefore respirable much longer.

Do you have anything to add about that? I know there's been some work, even before the pandemic, because it was used in -- it was required for sanitizing ambulances between patient runs.

DR. SALAMOVA: Um-hmm.

CHAIRPERSON SCHWARZMAN: And there were complaints from paramedics about acute health effects from exposure to fogged spaces, and presumably from having to do the fogging themselves. I wonder if you've just encountered any of that science, even though it's outside this -- the particular study that you did.

DR. SALAMOVA: We haven't -- we haven't had a chance to work with any of those application types. So the products that we've looked at were just sort of consumer products commonly used in homes, just the consumer sprays and wipes. I can see that the wipes had higher concentrations than the sprays. But again, that's different from what you're talking about. I think it's also important to know what kind of -- what kind of QACs or what kind of products are used in those foggers, you know. We don't -- we don't know.

But I think the way they are dispersed could create more lingering in the air and more -- maybe lead to more inhalation exposure than the products that are used

indoors just using the consumer products.

CHAIRPERSON SCHWARZMAN: Thank you for that.

I also saw material about people's exposure in hospitals, including people who did not use the products, but because they linger in the indoor environment, measurements at nurse's stations and in areas where a janitor was working, but not spraying them, but maybe mobilizing dust through sweeping and things like that.

DR. SALAMOVA: Um-hmm.

CHAIRPERSON SCHWARZMAN: But it all makes -- seeing your work makes that all make more sense.

I think Tom had a question followed by Veena.

PANEL MEMBER McKONE: Yes. Thank you. Really good presentation. So I'm curious if this work is leading -- I know there's not a lot of information about exposure pathways, but I'm wondering if there's enough early information to start hypothesizing dominant exposure pathways, inhalation, hand to mouth. I'm particularly interested like when a compound has a high K(OA), it's very -- it has a high preference for lipids, right.

So that would indicate that it's on surfaces. And if you -- your hands have lipid, you know, oils and things, it might be -- it might be retained on the skin more easily than compounds that aren't very lipid soluble.

In addition, it seems to be in the particle phase

probably less in the vapor phase, but that also suggests kind of the order of magnitude of the inhalation exposure, because we can calculate the air particle or surface particle partitioning. So again, this is -- I'm hoping that either someone already has begun this or we could be begin some, I wouldn't say, details or highly accurate exposure modeling but at least basing or building sort of the hypotheses that lead us to understand dominant exposure pathways, so we can start thinking about intervention.

DR. SALAMOVA: So there is some work. I know one paper that has looked at some of the exposure modeling looking at different exposure pathways, a paper from Li Li, which I believe was published either late last year or maybe earlier this year. And so in that paper, they have looked -- they've looked in an exposure model to look at different exposure pathways and they identified that dermal exposure and exposure from surfaces could be an important exposure pathway. They've looked at total of 22 QACs, I believe.

So I think the problem here is that there is so many different QACs with different properties, right? So we see this difference between the pattern in air and pattern in dust. So dust is obviously more important for less volatile QACs, like BACs. And we see now, although

up until now, there was this consensus that QACs are non-volatile, but we see that some of them are volatile and actually are found in indoor air, based on our exposure data. So I think that's something that needs to be more looked into.

We see -- I did not present this data here, but we see a similar sort of pattern with outdoor air. With outdoor air, we were able to collect vapor phase and particle phase contaminants separately. And we see a similar trend with BACs being more enriched in particle phase and ATMACs being more enriched in the vapor phase.

So I believe that inhalation also is an important exposure pathway for some of these QACs.

CHAIRPERSON SCHWARZMAN: Thank you.

Veena.

PANEL MEMBER SINGLA: Hi, Amina. It's really good to see you.

DR. SALAMOVA: Hi, Veena.

PANEL MEMBER SINGLA: Thank you so much for this great presentation and really important work. My question was around, if you saw any differences in exposure levels or patterns by age, or gender, or race and ethnicity within your cohort or if there's been any investigation -- other investigations of those kinds of trends, because I know for other chemicals, like flame retardants, young

children's greater contact with contaminated dust is hypothesized to be a more significant exposure pathway.

And I also -- you know, for other chemicals in the home, women are more often doing the cleaning and may have higher exposure, so I wondered if you had any thoughts on that?

DR. SALAMOVA: Yes, absolutely. That's a great question. We have tried to look into this, but in our data, we didn't see any differences. Our data was pretty homogeneous in terms of age all of our -- you know, it was all adults. We didn't have any children, because it was collected -- the samples were collected from a biobank at the hospital from surgery patients, so it was all adults. We did not see any differences in terms of -- in terms of between woman and man, or based on age, or any other -- any other characteristics, probably because we had a smaller -- a smaller data set, so that was probably the reason.

CHAIRPERSON SCHWARZMAN: Eunha.

PANEL MEMBER HOH: Hi, Amina.

DR. SALAMOVA: Hi.

PANEL MEMBER HOH: Hi. It's great work and it's very impressive. Is -- I'm curious about this could be -- you know, you may not know, but I'm kind of wondering, you know, we know that the chemicals are accumulating and

they're persistent, you know. So -- so I kind of wonder if you have -- you were able to try to differentiate something like, you know, when you have dust samples before COVID, after COVID-19, you know, you see the increased trend. But is there any possibility that these chemicals could accumulate in the dust over time? So this could indicate that longer use of these chemicals, this dust could reflect that accumulation impact effect?

DR. SALAMOVA: So remember that the dust were not paired. So they were not collected from the same homes before and during the pandemic. So in terms of accumulation or longer accumulation, that probably can't be ruled out, but it's -- it's also a limitation in a way, because we weren't able to compare the levels in the same homes. So there could be some other confounding factors, which contribute to the differences we see, but that's -- that's what we could do due to -- because of the limitations of the pandemic, in terms of sample collection.

CHAIRPERSON SCHWARZMAN: Elizabeth, I want to check in about questions from the audience.

DR. MARDER: We currently do not have any nor do we have any hands raised.

CHAIRPERSON SCHWARZMAN: Okay. Great. So we have about four more minutes before moving on for any

other questions from the Panel?

José.

PANEL MEMBER SUÁREZ: Hi, Amina. Thanks for the nice presentation. I just had a very basic question about the timing of the air samples in this case. They coincide -- I mean, by design, was it just randomly at any time of the day or did they coincide with soon after cleaning floors or whatever, how did you design that?

DR. SALAMOVA: So the air sampling and dust sampling overlapped. So the dust was collected at some point during the air sampling, but it wasn't linked to any specific events, like cleaning or anything like that.

The nature of the air sampling, that's why I mentioned that it's more complicated, that the sample needs to stay out for at least three to four weeks for us to be able to get good detection limits. And dust collection is pretty quick, so there was a difference in terms of sample collection time.

PANEL MEMBER SUÁREZ: Okay. So if I understand, so it's roughly a three week to four week average of the air sample that you're having there.

DR. SALAMOVA: Yeah. The air sampler stayed in homes for four weeks.

PANEL MEMBER SUÁREZ: Okay. Wonderful. Thank you.

DR. SALAMOVA: You're welcome.

CHAIRPERSON SCHWARZMAN: Any final quick questions?

In that case, thank you so much, Amina, for your presentation.

DR. SALAMOVA: Thank you.

CHAIRPERSON SCHWARZMAN: And we will move on to our next presentation. And I want to introduce Libin Xu, who's an associate professor at the University of Washington, where he started his own lab in the Department of Medicinal Chemistry. His research focuses on the role of lipid metabolism and oxidation in human diseases and the development of novel methodologies for the analysis of lipids, metabolites, drug -- drugs, and drug metabolites using mass spectrometry -- mass spectrometry techniques. Libin will discuss analytical methods to measure QACs in biomonitoring studies.

(Thereupon a slide presentation.)

DR. XU: Thanks, Megan, for the introduction. I hope you guys can see well, because I cannot see everyone else.

Only have the screen here.

CHAIRPERSON SCHWARZMAN: We can see you.

DR. XU: That's great.

So it's great to be able to visit Biomonitoring

California again. Last year, I was here. I remember that was the last time I ever traveled by air. So I really miss that.

But so today, I'm going to touch base on some of the thing I talked about last time, including metabolism, also some analytical methods. But I also want to talk about some of the newer data that we generated of human samples.

Let's get started.

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DR. XU: So I think Bill and Amina has done a pretty good introduction on the quaternary ammonium compounds or QACs on their structures, and their usage as disinfectants, pesticides, preservatives, and they're regularly used in a variety settings. And nowaday, because of COVID, the use has, you know, times -- probably increased many times. And including the wipes and also spray, we mentioned about the potential inhalation exposure. Spray could be an important route, because it's being used quite often, and other kind of medical products, eye drops and also dairy products.

These are the structures, that Bill and Amina has mentioned. I won't go through them all again, but I want to point out that this talke we're going to focus on the benzalkonium chlorides, which has benzyl, dimethyl, and

alkyl chain, different chain length and also didecyldimethyl ammonium chloride, which has these dialkyl chains and dimethyl groups.

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DR. XU: So first of all, I want to introduce the method we're using. We're using a targeted liquid chromatography-mass spectrometry method, which is similar I think with Amina's method, which was also a targeted methods. It's a reverse phase column separation with a solvent combination of buffer with formic acid and also acetonitrile. The total run time for these pairing QAC compounds are, we think, eight minutes.

And we have synthesized deuterated labeled standards as internal standards, so we add these standards before we process the sample that we'll account for on the potential sample loss during the process and also allow the quantitation to be very accurate. And these are the mass transition that we used for the different compounds which are specific to that particular compound.

And so this is something I mentioned last time, like before, because there's no really human exposure data, and so we kind of outsourced through BioIVT to get -- obtain a hundred random human plasma samples. And we did that kind of highly study we found that, you know, for 25 to 47 percent have detectable level of QACs. And

for some individual who has pretty high level, we -- including you know about nine percent could have micromolar concentration of these QACs.

But we do recognize the limitation of this study, because the samples were not collect by us. And then it could be -- there's a possibility for contamination during their collection process. But I'm going to touch on some newer data on collaboration with Terry Hrubec and on some of the samples that, you know, collected by themselves and also I think controlled very well. So -- but regardless, we can see from the sample that the QACs are prevalent. That has varied levels among individuals.

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DR. XU: So our lab has done some, you know, early study. Like I could -- it's recent, but nobody has really looked at the metabolism by human enzymes. So we look at the metabolism by human cytochrome P450s, the main detoxifying enzyme in our liver. So here we use the benzalkonium chlorides as examples.

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DR. XU: And we have reported in the last year. Basically, we have identified enzyme cytochrome P450 4F11, 4F2 that will make omega-hydroxylation products. And the 2D6, 4F12 will make omega minus one hydroxylation products. And omega-hydroxylation products can be fully

converted into omega-carboxylic acid. And where the other one, you know, omega minus one can be converted into ketone, and both of these can be converted into this diol dihydroxy products. And so we have made synthetic standards for C10 BAC to confirm all of this diol transformation pathway.

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DR. XU: So this is some recent, you know, mechanism. We understand that after they form the primary carboxylic acid products, they can actually undergo beta oxidation, like fatty acids, that would reduce two carbon at a time to form a series of carboxylic acid products.

So this is important, because that relates to some of the metabolites we have seen in human urine. We can see it later.

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DR. XU: So these are some of the chromatogram that we use to monitor C10 BAC-derived metabolites. Thes are untargeted methods. They hydroxy products, the dihydroxy, the ketone, and the omega-carboxylic acid.

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DR. XU: And I'm showing here is actually a mouse study where it exposed the mouse by diet at this level 120 micrograms per gram per day of QACs containing BACs and also DDAC. And following actually Terry Hrubec's

protocol, what we see is this is looking like -- looking at kidney tissues we see on the compounds in there. And we see -- I'm showing here metabolites of C14, but we also see other metabolites too of C12 and C16 BAC.

Interestingly, we also see hydroxylation metabolites of DDAC. Although, we haven't fully characterized the products of the DDAC yet, but we think the oxidation also occur on the long alkyl chain, which we're in the process of characterizing those.

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DR. XU: So in a separate study, we look at, you know, again, the mouse fed on -- actually, in this case, we use a deuterated labeled C13 BAC, because we find that there may be some contamination from the environment that could obscure our analysis. So with that with D7 deuterated labeled one that we make sure the only thing we analyze or definitely coming from the diet that we fed the mice.

So we see again -- you can see for C16, we see the parent compound, also omega-hydroxy, omega-carboxylic acid metabolites. Very interestingly is that these are in feces by the way. And we also see a series of beta-oxidation products from this omega-carboxylic acid. The n equals five, that we could be equals to the alkyl chain of 14, that would be 12, and then, ten and eight,

even six. So they are, you know, undergo, what we thought, you know, of metabolism by cytochrome P450 followed by the beta-oxidation products. So this is an indication that the QACs are absorbed and also they are metabolized by liver, and then they are excreted back into the intestine and then into the feces.

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DR. XU: So this is just a summary of our, I guess, very fairly conservative estimation of limit of detection, which we can reach our limit of detection of under 0.1 nanomolar and it convert to nanogram would be in the -- from ten to -- up to 90 nanogram per liter.

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DR. XU: So next, I'm going to talk about some other newer data that we have done on human samples.

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DR. XU: The first study is a direct collaboration with Terry Hrubec at Virginia Tech. And so they did a blood sample collection at Blacksburg, Virginia, which is a college town, and participants over -- 18 years or older. Total is 43 samples collected. And the way we process the samples are like we're spiking deuterated BAC, benzalkonium chloride, internal standards. We did a lipid extraction actually, because most of these QACs we analyze are very lipophilic, using Folch solution.

And then after drying those, we reconstituted them into LC solvents. And then we do the targeted LC-MS/MS analysis.

So this manuscript is now in pre-print. We're currently doing the revision. Hopefully, that can come out soon.

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DR. XU: So just to show you what we see, just picking three samples from the collection, sample 4, 17 and 38. You can see showing the 12, 14 and 16. In these samples, they have varied levels. It depends on the individual. And even the distribution for the different compounds is a little bit different. We do see DDAC as well, which is not shown here.

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DR. XU: And this is a summary of the data we have seen. It's from -- you know, for all 43 samples. And different color shows different compound, like 10, 12, 14, and 16 BAC and also DDAC. We can see some of the highest level can reach is sixty-some nanomolar for one individual and total QAC in that individual is probably reaching from 100 to 200 nanomolar. And there's another pretty high individual. And there are a lot of low nanomolar concentration among -- on other individuals. But we can see the distribution range is quite high. And some individual could -- actually has really high level of

these QACs in their blood.

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DR. XU: So next I'm going to talk about some of the pilot study we have done on human urine samples. So after last year's meeting, I've kept in communication with Nerissa Wu from Biomonitoring California. And so we started this pilot project to look at human urine samples.

For one, it's that human urine is much easier to collect, particularly during COVID. You can avoid in-person interaction and you can still get urine samples. So these are, I think, from the early staying at home order, the plan collected samples.

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DR. XU: So first I want to touch on the, you know, method, which is -- you know, we settled on this method. It seems to be working pretty well and also very straight forward to work out the samples.

Basically, we add ice-cold acetonitrile and with deuterated standards already in there. And then we chill them on ice to precipitate into proteins. And you do centrifugation, and then take the aliquots, supernatant it out, and concentrate them down under vacuum, and then we finally reconstitute them into LC solvent. Then do LC-MS/MS analysis.

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DR. XU: So this is what I show is from one human urine samples and the metabolites we have seen. We didn't see parent compounds in this -- in this urine sample. On the top chromatogram, are from this urine sample, we can see these are all carboxylic omega-carboxylic acid metabolites with a 12, 10, 8, 6, and 4 carbon chain. And the concentration ranged from one to 16 nanomolar, and total is about 45 nanomolar.

So if you compare this carboxylic acid metabolite profile with this C16 BAC incubated products from human hepatocytes, we can see the matching of this omega carboxylic acid metabolites with this profile. But in the human urine, we didn't see 14 and 16. So we are guessing the longest chain in this individual probably is C12 that's been exposed. But we're not sure about parent compound of 10, 8, 6, whether they exist or not, because as I mentioned earlier, the carboxylic acid can undergo beta-oxidation to lose two carbon, and at the time, eventually reach to these potential products.

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DR. XU: So in the last part, I want to, you know, touch base on some of the literature data on QAC disposition that was done in animal models. I hope to give you a whole picture of their disposition, even though there are differences between, you know, animal, like in

particular mouse, and rats, and humans, because mouse and rats do metabolize much faster. But I think this is some indication, that you can potentially extrapolate it into some human disposition data.

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DR. XU: So these are a couple of studies in early 2000s from -- in rats after IV or oral intake. The top one is from IV injection, seven microgram per gram injection. And the rats were sacrificed 30 minutes later. So you can see the distribution of BACs after this periods. It's kidney has the highest level followed by lung and spleen. And the blood level in serum is actually pretty low and liver level is also pretty low.

But we know these compounds can be metabolized well by liver. And if you look at the -- oral intake data from 115 microgram per gram of intake, and the rats were sacrificed 24 hours later, you again see the kidney accumulate the highest level of these compounds, followed by lung, and liver is pretty low, and the blood is the lowest.

So this is suggesting like, you know, blood may not be the highest level that you can see for these compounds. And also, if you will look at our human blood sample, also Amina's data on human blood samples, that could be an indication in other issues, like kidney or

lung, maybe they have even higher accumulation, for whatever reason. It could be because of their uptake. It could be because of their limited metabolizing capability.

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DR. XU: So another data I want to present here is some radiolabel study that is cited often by EPA and FDA, even though these are unpublished data, but some FDA documents, for example, in this particular document cited this and included the exact number.

And also this recent review also cited this data. So these studies were done in rats and then fed -- feed the rate with C14 labeled, benzalkonium chloride either by IV or oral dose at 10 milligram per kilogram per dose. And so the feces, urine were collected throughout and also tissue were harvested.

So as you can see, even with IV dosage, there's a lot of fecal excretion and also urine excretion. It's 30 percent remain in the tissue. So this is an indication that urine and feces excretion are major routes, particularly for fecal excretion.

And for oral doses, as you can see, you know, fecal excretion is predominant, followed by urine, and tissues normally range is one percent or less. That is, you know, after a week or two collection of samples already.

So what I want to really point out in this data is that the -- from the fecal samples they have -- they find -- they find like about 65 percent are parent compounds while 35 percent metabolites. They have indication that metabolites are hydroxy or hydroxy-ketone metabolites. But really, they didn't figure out the structure of those metabolites. But we know now those primary metabolites could be hydroxy compounds, could be ketone, and could be carboxylic acid. And we know those are formed from human cytochrome P450 that are in the liver.

I think that's a very, you know, important, you know, concept here is that this compound do get absorbed, and they do get metabolized. That's how you can see these metabolites. That's it -- after excreted back into the intestine.

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DR. XU: So I hope to give you a whole picture of the, you know, disposition routes of QACs. They could be -- have intake through oral intake, but it could also have intake through inhalation and possibly skin surface. I viewed inhalation could be very dangerous routes of intake, because lung has very low metabolizing capacity, so that means the compounds would likely enter the systematic circulation without much metabolism. So either

way, if they are intake, we know they are absorbed and then we know liver metabolize them, and we know liver actually secrete both parent compounds and metabolites back to intestine through biliary secretion and that can go out into feces or they can actually re -- be reabsorbed back to the circulation system.

So -- and then through the circulation they can reach to different tissues, including the kidney. And in some other unpublished data we have find some organic cation transporter can actively uptake these compounds and the kidney and has expressed a major form of this.

And kidney, either they can retain the compounds or they can excrete them out through urine. From the data in animal, there seems to be some indication kidney may not be able to excrete them very efficiently. That's why they have accumulated highest level of these compounds.

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DR. XU: So just to summarize, I hope you can understand that these compounds as a foreign compounds we do metabolize them. Our body has the machinery to be able to metabolize them. And we can quantify both the parent compounds and metabolites very sensitively and a targeted -- in a targeted way from a variety of biological samples. And they are absorbed in human blood and urine samples and we see metabolites in the urine as well.

And also suggesting the fecal, urine, or blood could serve as good biomonitoring samples. But if the blood collection is, you know, troublesome or not feasible during the COVID, but fecal and urine sample would be very good samples too to monitor for their exposure level in humans.

Just to acknowledge my group, this is pre-COVID. I think I showed the same picture last year. So, Ryan, who did most of the metabolism and analytical work on QACs. And Josi and Vanessa did the animal work.

And I want to thank the funding support. We have a pilot grant from the School of Pharmacy to start this -- working on this project.

And I'd be happy to answer any question that you may have.

Thank you.

CHAIRPERSON SCHWARZMAN: Thanks so much. We appreciate that.

We have 15 minutes for -- actually, we have -- if we need the time, we have just a little bit more because you finished a little early for questions for Libin from both the Panel and the audience.

Yes, Oliver.

PANEL MEMBER FIEHN: Yeah. I wondered if you also had used accurate mass analysis to see if there are

other types of modified versions, like glucuronidates or other types of metabolites that one could detect?

DR. XU: Yes. Glucuronidation is very possible for metabolites. We have started to look at those secondary metabolites. We have seen some in human hepatocyte incubation, for example. We haven't specifically looked for that in the urine samples. We don't have synthetic standards, but we have standards from like incubation with human hepatocytes that we have some idea where they are. Yeah. Very good points. They could have the secondary metabolite that allows them to be excreted more efficiently into the urine.

CHAIRPERSON SCHWARZMAN: Other panelist questions.

I will -- let me read a question that was emailed in from the audience.

In slide 15 -- oh, sorry. I should say this comes from David Dabney at Stepan Company. In slide 15, you show that for most blood samples the total quantified QAC is at or below 10 nanomolar. Can you comment on your prediction of the fraction of the QAC that is free and bioavailable in these plasma samples and how much is likely bound to plasma proteins and thus not biologically active, given the known properties of QACs to tightly bind to organic materials. Do your methods differentiate free

versus plasma-bound QAC?

DR. XU: Our method doesn't differentiate them, because we did extraction on the whole blood samples on the QAC potential be extracting into the lipid fractions. But that's a good point, that the compounds they do tend to bind to protein, you know, in the plasma, for example.

We're in the process of looking at that, you know, like how do they partition between say albumin versus just free environment in the solution.

I think that's also a good indication that these compounds could linger in human body for longer time, because they have this tendency to bind to proteins, albumin like, and that could actually slow down the metabolism. And -- so which could be an indication of why, you know, they could be detected, for example, long after exposure in animal models. However, in the -- if you do the -- in the many reactions, their consumption are done in 30 minutes, so for example.

So I think that's a -- you know, that's a very good point, but it does -- I think the longer half-life doesn't provide, I guess, the opportunity for the compound to be systematically circulating to different tissues.

CHAIRPERSON SCHWARZMAN: Thank you for that.

Other questions from panelists?

And Elizabeth, let me check in about -- okay. I

just saw that Jenny has a question and then I'll check in with Elizabeth. Let's go that way. Go ahead, Jenny.

DR. MARDER: Jenny, I don't think we can hear you.

You can try again.

PANEL MEMBER QUINTANA: Hi. I think I'm unmuted now. Can you hear me?

DR. MARDER: There you go.

PANEL MEMBER QUINTANA: Okay. Thank you for your very, very interesting presentation and all your hard work that you've done on this issue. So it just sounds like my naive takeaway from what you presented is that you would think that urine would be a better way biomonitor rather than blood or is that too simplistic of a takeaway?

DR. XU: Well, I think urine, during pandemic, may be easier to collect, that you don't have to go in person to collect it. It's more convenient. It definitely is -- it will be good to have blood, because the profile I think will be different. What you, in urine, will mostly observe is very polar metabolites that are water soluble excreted out in the urine. But in blood, we may see the parent compounds or other less polar metabolites.

Yeah. But for convenience, urine is easier to collect. I would say fecal sample would be the best,

because I expect fecal sample to contain the majority of the information. That's because of the excretion routes that we have seen from -- I guess, from animal models.

PANEL MEMBER QUINTANA: Thank you.

CHAIRPERSON SCHWARZMAN: José.

DR. XU: I guess you're still muted.

CHAIRPERSON SCHWARZMAN: Yes, I was waiting for José to speak.

PANEL MEMBER SUÁREZ: There. Sorry. For some reason, the organizer muted me, I think, while they were trying to unmute me.

Okay. My question is do you have an idea of what the variability, in other words, like what the within individual variability and how that may compare to the between individual variability say in urine of measurements of these metabolites?

DR. XU: Yeah. Good point. I think, first of all, the exposure could be very different between the individual. And another thing is I want to mention, many of the enzyme they're metabolizing these compounds. Kind of highly polymorphic. And there are certain individuals that are poor metabolizers, that means -- that means they could affect their, you know, half-life in our body. It could affect whether we efficiently clear them in our body.

The CYP2D6 is one of the best known, highly -- has a very high range of metabolizing capacity that vary among different individuals.

PANEL MEMBER SUÁREZ: Right. So, I mean that -- I mean, that's correct. So it's a link between half-life, the exposure -- recurring exposures and then you have metabolism all playing a role in that. I would -- do you have any sort of information. My naive, I guess, guess would be that the variability in blood would be much higher than that of urine. And I suppose the methods of quantification in urine may be a little harder, because the concentrations, I would think, would be substantially lower in blood than they would be in urine. Can you comment a little bit on that?

DR. XU: You're saying in the urine be lower than the blood?

PANEL MEMBER SUÁREZ: The other way around. In the blood would be lower than in the urine, as you anticipated more concentrated --

DR. XU: I think -- I mean, from our data, the collaboration with Terry Hrubec and also the urine sample, we think the blood sample probably has higher level overall, particularly of parent compound levels. Urine, like I said, what we observed, are kind of terminal metabolizing products, we think. Yeah.

PANEL MEMBER SUÁREZ: And just to follow up on that question. With regards to the metabolites, are there any sources of exposure to the metabolites that are not necessarily correlated with the exposures to the actual compound that we should be aware of?

Sometimes this would happen, like in the pesticide world, we're measuring, for instance, dialkyl phosphates where they are a marker of exposure to pesticides, but also if people are exposed to dialkyl phosphate, not actually the pesticide, that they would have detection, of -- you know, the test would come out positive -- positive value, so they're actually exposed to the metabolite not to the actual pesticide, which kind of means something different when it comes to the toxicity of the chemical, right? Is there any notion about that perhaps?

DR. XU: Okay. I think you mean is whether this compound can, you know, somehow transfer into the metabolites outside human body.

PANEL MEMBER SUÁREZ: (Nods head.)

DR. XU: Yeah. So from my current knowledge, there's no evidence for that. I think from some of environmental studies, this hydroxylate -- terminal hydroxylated products or carboxylic acid products are not some deg -- of the degradation products that's observed in

the environment say. And so -- and I think some of the people have argued whether our gut microbiome can metabolize these compounds.

From my understanding, it's got microbiome bacteria. Because it's anaerobic environment in our gut, most of the transformation actually not oxidation in the metabolism in our gut. And these products we observed actually match really well with the human cytochrome P450 metabolism pathway.

PANEL MEMBER SUÁREZ: Um-hmm. Thank you.

DR. XU: Yeah.

CHAIRPERSON SCHWARZMAN: Thanks for that.

Veena, I see your hand and then we have a couple of staff comment questions and a couple of public ones. So please, go ahead, Veena.

PANEL MEMBER SINGLA: Thank you. Thank you so much for this presentation. I wondered if you have thoughts on factors contributing to the particularly high exposures in some of the individuals. Amongst the 43, you've already mentioned metabolism differences could play a role. I wondered if you had thoughts on other factors.

DR. XU: Yeah, I mean, certainly I think some high exposure occupation, janitors, you know, health care workers, they could be of really, really high risk, particularly I think in the environment where you really

spray these compounds often. Like I mentioned, you know, inhalation this route of exposure go through the lung. The lung doesn't have as much metabolizing capability.

And that means you -- these compounds will gain circulation without being sort of detoxified. I would say, you know, those are probably really higher risk population in here, where the spray are used often. I know during the pandemic, a lot of environment used this and also used in the closed environment, in a school, you know, some.....I know.

And the spray I think that you probably heard about the -- some of the Microban, those kind of things, like on the TV commercial. I think those are kind of probably higher threat exposure route at this time.

And also, I think last time there were some discussion on the asthma risk associated with occupational exposure. So that -- I think that certainly increased that part of the risk too.

PANEL MEMBER SINGLA: Thank you.

CHAIRPERSON SCHWARZMAN: Thanks.

We have a couple of staff comments or questions. I think Nerissa.

DR. WU: Hi. I just wanted to add -- Thanks, Libin. That was great. But we mentioned the intraprogram pilot study. This is a protocol we have for doing method

development and demonstration. And as part of the samples that Libin already described to you, we do have a small group of paired fecal urine samples from clinical workers. And it's a very small number. And fecal samples are not anybody's favorite way of biomonitoring, but we hope that it will add to this body of data and give us a better sense of the proportion of urine versus -- this fecal metabolite -- rather excretion.

DR. XU: Yeah. We definitely look forward to looking at those samples. I think they are in pipeline out for analysis.

DR. WU: Awesome.

CHAIRPERSON SCHWARZMAN: Thanks.

And Amina had a question or comment.

DR. SALAMOVA: Yes. Thank you. Thank you, Libin for a great presentation. I'm glad to see that we're sharing some interest in biomonitoring of QACs.

I was wondering if you are planning, or maybe you have, looked at ATMACs in blood, because we do see almost 50 percent contribution from ATMACs in our blood samples. So they are definitely present in equal quantity to BACs in the blood samples. And I'm afraid if you don't look at them, you'll miss that portion of the blood.

And I understand that ATMACs can be metabolized more slowly in the body, so that can be a reason for the

higher presence in the blood. So do you have any comment on that?

DR. XU: Yeah. Yeah. Thanks Amina for that advice. I think after hearing your talk, we definitely will look more in the ATMAC compounds. Currently, they are not on our targeted method, but we do, you know, high res mass spec analysis too. So potentially, they are in some of our, you know, profiling, you know, spectra that we can fish out. But definitely I think we'll try to add that into our targeting method, so we can get a more accurate quantitation.

Do you have, I guess, deuterated label standards for those compounds?

DR. SALAMOVA: I can't remember off the top of my head, but I can check and get back to you. I think we do.

DR. XU: Okay. Cool. Great. Yeah, we'll be in touch.

DR. SALAMOVA: Yeah. We'll keep in touch. Thank you.

CHAIRPERSON SCHWARZMAN: Thanks.

Elizabeth, can you help us with the public questions from the audience?

DR. MARDER: Absolutely. One of them was already covered. Just very briefly, we had a question from Guomao Zheng about did you analyze some other metabolites e.g.,

the hydroxylated QACs in urine? I think that was covered, unless you wanted to add something else.

DR. XU: We do look for hydroxylated products in urine. We didn't see that. Yeah. That's why I say like in urine, likely those are like very polar metabolites that are excreted out through the urine, and the carboxylic acid are kind of the terminal products. Very polar. Highly water soluble. That's probably why we see those predominantly in the urine.

DR. MARDER: Thank you.

And then another question, have you noticed any contamination issues when analyzing the parent QACs? This is from Amy McDonald, University of Calgary.

DR. XU: Yes, it is a problem. So we always draw blanks. Like including when do sample processing, we do a blank extraction and carry that through. So that give us some baseline level of what kind of signal we might see for that particular batch of samples.

Yes, it is a problem and so we only view signal that's, you know, above or several times above the baseline level to be, you know, comfortable say that's detection. I think that's -- that's an issue for this. I think Amina's data also showing that there's always some background levels around.

Also, you know, that's another indication that

these kind of compounds are really used very prevalently. You could be in many of the southern production for example, like in -- for our LC-MS analysis and it could be in many of the containers too. So -- trace levels. So I think it's certainly everywhere. Yeah, it's very -- yeah. It would be a good practice to do that blank workup and also run the blank every once in a while during your rounds.

DR. MARDER: Okay. One more question and one request to speak. The question is a note on slide two content that -- about the statement that no public data on QAC exposure levels in humans and a 14-year old EPA document the re-registration eligibility decision document being cited. Do you believe that all the exposure estimates in U.S. EPA's 2017 workplans are some how quote not public or not relevant? This comes Aron Pollard of Pilot Chemical.

DR. XU: I would say, the cited data I think is probably also -- you know, I've cited those for their usage, you know, where were they used. I haven't seen any actually published data to human exposure level in blood or in other biological samples. Yeah, so I think an EPA document could cite some of those numbers, but I really didn't see those original data, like in the -- where that is from.

Yeah, and -- yeah, I mean, there's -- in the public domain, I haven't seen that. But if you have those data, please let me know.

DR. MARDER: Okay. And there are now two for requests to speak, Meg, if you have time for one or both. I will unmute the first person. So June-Soo Park, you're first. There you go.

DR. PARK: Thank you. Thanks again, Dr. Xu for wonderful and inform -- very informative talks.

My question may be a little follow up to what Dr. Fiehn asked earlier. I know, this may be likely very simple and naive one. I remember the -- you showed the -- I saw some of your observation on the QAC distribution among organs, like lung, kidney, liver, and blood, more prevalent in the lung and kidney system. I'm just trying to get some hint how much they exist in the -- in free form or conjugated general in -- in general in blood or urine samples. I'm sure the -- there will be also the -- you know, the compound-specific, also the people-specific, you know, also the -- how recently they got exposed.

But I'd like to get some idea what kind of free form I can expect from the liquid samples, like blood and urine samples. I don't -- I know the -- have you done any simple experiment like enzyme incubation? I'm not sure. Yeah.

DR. XU: Yes. So we have done human liver microsome incubation. But those are -- those are in vitro experiments. They consume the QACs really fast.

And then for tissues and the dose, the study I cited, they're measuring the parent compounds. I don't think that they - I guess at the time of their study - didn't know what kind of metabolite to look for. I don't think they measure any metabolites in those studies.

And we know that the parent compounds are substrates of organic cation transporter, for example, that's expressed in kidney that will uptake them. So that could be, you know, one of the reasons they are higher in the kidney. But we don't know, yet, whether the metabolites are also the substrate of organic cation transporter.

CHAIRPERSON SCHWARZMAN: Thank you, Libin. We need to break now for our transcriber. And so we will have a chance to address other questions maybe during discussion at some point. So we're going to go to a break now. Thank you very much for -- Libin, for your presentation and your discussion. And we'll resume at 2:50 p.m. Thanks.

DR. XU: Sounds good. Thanks.

(Off record: 2:37 p.m.)

(Thereupon a recess was taken.)

(On record: 2:50 p.m.)

CHAIRPERSON SCHWARZMAN: I will restart the session here. I -- we are going to have two presentations now before opening our session on considering QACs as potential priority chemicals.

So I want to introduce Keith Hostetler and John DeSesso, understanding that we might not have John on quite yet.

Keith is a Senior Managing Toxicologist in the SafeBridge Regulatory and Life Sciences Group of Trinity Consultants. Prior to becoming a consultant, he spent more than 20 years in the specialty chemicals area with multi-national expertise in toxicology and regulatory affairs. He -- Keith holds a PhD in pharmacology and toxicology from the Medical College of Virginia at Virginia Commonwealth University.

And John DeSesso is a Principal at Exponent, Inc., which is a scientific and engineering consulting firm and a professor at Georgetown University School of Medicine. He has over four decades of experience in the areas of developmental and reproductive toxicology, embryology, anatomy, and risk assessment.

John earned his PhD in anatomy and teratology from the Medical College of Virginia, which is now Virginia Commonwealth University School of Medicine.

So Keith and John will present on evaluating the safety of QACs.

(Thereupon a slide presentation.)

DR. HOSTETLER: Okay. Thanks to the group for inviting us to be part of this. I'm struggling now. I was expecting to see my slides closer to me in front of me. Maybe I got the -- okay.

So as I mentioned, we're going to be covering about 40 year's worth of work here in the next 20 minutes, so we're going to have to move fast and I'll turn it over to my colleague John DeSesso momentarily.

We've already been talking about -- through a number of presentations, about QACs, especially the disinfecting QACs and their important role being named and being included on EPA's list because of their efficacy against pathogenic organisms. They're unique and favorable, in that they perform at very low concentrations. And when used as directed, over the years, they've proven to be safe and effective when they are used as directed.

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DR. HOSTETLER: They're registered around the globe for a number of uses. And that's based on the extremely robust datasets that have been developed over the years and reviewed by the Authorities.

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DR. HOSTETLER: We talk a little bit about a couple of different ways to use these. I have a slide here to just sort of focus in on, well, two user groups. First, maybe the residential, the consumer side, where QACs are used and approved for use in food sanitizing -- or food contact surfaces. About a teaspoon full of a concentrate in seven and a half gallons, to give you a sense for how low they are and still effective, and more in a occupational setting, for example, in a health care setting, concentrations of 3,000 ppm, that's in diluting about a teaspoon full in two liters of water. So it gives a very strong disinfecting health care grade product. In some of these cases for the more concentrated uses, of course, personal protective equipment is indicated on the labels.

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DR. HOSTETLER: As I mentioned, over 40 years, these compounds were introduced. I think we saw that in Dr. Arnold's presentation back in the 40s approximately. But they've been studied continually for that time by the regulatory authorities. They require far more stringent than peer review. They require guideline-compliant studies that have to meet a range of demanding properties before they're accepted and can be used for human risk

assessment.

They require studies in relevant species that are predicted with human health endpoints. And when these reviews have been conducted and they continue to be conducted on an ongoing basis, they've been shown both by U.S. EPA and by the European Chemicals Agency to be approved for their current uses with no restrictions.

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DR. HOSTETLER: Interestingly that's part of the -- what makes them unique as well, is that they're not systemic toxicants. They're not known to cause any adverse effects distant from where they actually touch tissue. If you give them orally, they cause gastric irritation. If they're applied dermally to the test animals, they can be irritants in a high enough concentration, even corrosive, but these are at high concentrations. The no observed adverse effect levels is what the EPA and ECHA use to ensure that the concentrations in the dilute products that people are being -- are using and potentially exposed to are safe. I'll highlight that QACs are not on any California Proposition 65 list.

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DR. HOSTETLER: Dr. Arnold mentioned, and it has been well determined, that QACs in the environmental fate

are well understood. They bind to sediment. Predominantly, they do get removed from sewage treatment plants and that improved with the Clean Water Act and improved wastewater treatment performance.

They do not volatilize. These are non-volatile substances. They do not volatilize into the air. That's a fact that's known, that's unquestioned. There has been tests on dozens of species of aquatic both chronic and acute data. All that's taken into account when conclusions are drawn about ongoing safe uses.

I listed here the criteria for priorities that was discussed at the beginning of today. And I note some general observations. U.S. EPA from an exposure potential estimates that unintentional but possible dietary exposure is less than a half a milligram -- less than a quarter of a milligram per kilogram body weight per day.

Dr. Salamova, from one of her publications, talked about dust, has quantified dust and estimated dust ingestion of far even below that. And we see from Dr. Arnold's presentation low concentrations, micrograms per liter, in wastewater treatment plants.

QACs are non-carcinogenic. They're not developmental reproductive toxicants. Dr. DeSesso will cover that endpoint in some detail. Where concentrates are handled, personal protective equipment is required.

There are -- they can be detected, as we've spent a lot of time too talking about detection. I will point out that there can be as many as several hundred similar compounds with similar molecular weights. And these have to be very carefully validated methods when it comes time to quantify. So they're not -- they don't seem to be similar to other products or other substances that are listed on your priority monitoring list.

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DR. HOSTETLER: I mentioned too, Dr. Arnold's work was very well received. We agree and believe that that's a fair representation. You can detect them in sediment. They're not detectable in surface waters. They don't migrate into drinking water. They have been tested. They're typically found in the parts per million, parts per billion or lower concentrations in the environment, and these are well below any concern levels for effects on species.

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DR. HOSTETLER: In terms of exposure, I think there was a question about exposure patterns. I would invite the Panel to spend some time with EPA's 2017 workplans for ADBAC and DDAC. These spend quite a bit of time detailing exposure patterns, how people could be exposed to these substances.

And in that, EPA identifies an acceptable daily ingestion of less than a half a milligram per kilogram per day. From Dr. Salamova's toddler estimation in her paper, this fraction of an exposure is some 700 times lower than that. Keeping in mind, this is a safe dietary exposure level based on all the cumulative robust data that's been submitted. Again, calling for research that there's urgency around risks associated with increased exposure when we're still talking about parts per million in dust seems a bit unwarranted.

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DR. HOSTETLER: So the overall valuation has been considerable. There's lots known about human exposure potential. There's tons of data of well designed, guideline studies that identified no risk levels and safe uses. And these are approved and used around the world, because of this robust data package.

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DR. HOSTETLER: Time doesn't permit me to go through all of the endpoints from a recent ECHA review, but this is an example. So in the appendix, the slides that you all have, you can see all of the endpoints that were looked at by the European Chemicals Agency. I highlight developmental toxicity, because that's an element and a potential endpoint that has garnered some

attention. Because of that, an expert panel has been convened to conduct a more rigorous and systematic review of both published and unpublished results. Dr. DeSesso chairs that expert panel. And if he's available to talk, he's going to take over the presentation from here.

DR. DeSESSO: Well, thank you very much, Keith. Can you hear me?

DR. HOSTETLER: Yes.

DR. DeSESSO: Yeah. Okay. Fine. Thank you very much Dr. Hostetler.

So the -- recently, over the past six or seven years, a series of papers have been published, which alleged that ADDAC -- ADBAC and DDAC cause reduced fertility and neural tube defects in rats and mice. And as Dr. Hostetler has mentioned to you. These two chemicals have been used for over 50 years by -- and they've been evaluated by multiple regulatory agencies and considered to be safe when used as directed.

So as a consequence, a teratology working group was empaneled to assess all of the developmental and reproductive data for these two chemicals and to ascertain whether these substances actually do cause developmental or reproductive effects.

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DR. DeSESSO: So I -- in order to this, the Panel elected to do what's called systematic review. And for those of you who don't know what a systematic review is, briefly, it's an attempt to objectively assess the scientific evidence to clearly -- a clearly formulated question, which in this case is do these chemicals cause reproductive or developmental toxicity.

And it uses a -- an explicit and transparent well defined methodology to do this. These are used most for the identification of the papers and reports to be reviewed, as well as selecting the appropriate ones to analyze and then to critically appraise them and use only the most relevant research to draw conclusions.

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DR. DeSESSO: So what we did was we did an automated literature review of the worldwide literature for using the names of the chemicals - ADBAC, DDAC - as well as benzalkonium chloride and their CAS numbers, and combined them with a variety of terms related to reproductive and developmental toxicity.

And our search revealed about 789 potential articles. We reviewed the abstracts and titles of the culled list and came down to eight in vivo laboratory studies that were performed in mammals.

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DR. DeSESSO: Among those eight studies, we found two chapters that came from a -- from a dissertation. And that dissertation was available online. When we looked at the dissertation, we found two additional chapters in that dissertation that had been written up in manuscript format, but had not yet been published. And so those are included in those eight studies that we wanted to review.

Now, in addition to the worldwide published literature, we also obtained safety studies for ADBAC and DDAC, which were supplied to the working group. And this constituted an additional six safety studies, plus four dose range finding studies, which we sort of subsumed under the definitive studies that we received.

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DR. DeSESSO: Now, in order to assess the quality of the -- and to be unbiased in the way we would do this, we used a software program called the ToxRTool method. It was developed by the European Centre for Validation of Alternative Methods, that's ECVAM. And it was -- the methodology is published on the open literature -- in the open literature and it's available on the net.

And what this series -- what this does is it asks

a series of yes/no questions that you can answer either yes as a one or no as a zero. And the computer program keeps track of the yeses and noes. And it also keeps track of the topic areas in which these are -- where these are supposed to take place. And at the end of this thing, they evaluate each of the different topic areas and some of the scores, and categorize the studies into one of three categories. The best category, category one, this study was considered to be reliable without restrictions. Category two, they're reliable, but there are some restrictions, and the third category, as ones that are not reliable.

Now, it's important to recognize that when we say they're reliable and all this, that this is for the purpose of assessing potential risk. All right. So that's -- are these good for risk assessment?

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DR. DeSESSO: So the results of our ToxRTool analysis, we found four studies that were in category one, two studies that were reliable with restrictions in category two, and eight studies that were considered not reliable. The two studies that were considered reliable with restrictions were among the unpublished studies. They were studies done in rabbits back in the early 1990s.

And at the time they were performed, they met regulatory guidance.

But recently, the number of rabbits that are to be used in studies are -- has increased. And for that reason, we elected to downgrade the -- those studies to category two, because they don't meet modern standards.

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DR. DeSESSO: So the big thing to consider, I guess, is to talk about the studies that were in category three. And what these -- in those -- within that group of five -- of eight studies, five of them are studies that have alleged reproductive and developmental effects of ADBAC and DDAC. And I want to discuss why they were considered to be not reliable.

In general terms, there are numerous studies for risk assessment purposes with these studies. Many of the findings in the studies are told more as anecdotes than they are as experiments, so they -- many of them don't have really rigorous scientific methods for the experiments. And oftentimes, they use non-standard methods, which were not really well described and so it's difficult to understand what was done and how it was performed.

So what I want to do next is just as examples

talk about just three of the concerns so you get a flavor for why these things were different. And the three topics will include the -- what the exposures were under the experimental conditions, which use ambient exposures; how doses were calculated in those studies in which materials were given by diet; and to talk a little bit about the terminology used by the authors when they described their findings.

So the next slide --

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DR. DeSESSO: -- we'll talk about the ambient exposures. And the ambient exposure conditions as provided by the authors were animals that were in animal rooms, in which a cleaning or disinfecting agent used a combination of ADBAC and DDAC in the -- in the -- in its formulation. In no case where the -- were either of these chemicals measured or identified in maternal tissues. That would be in blood, liver, or placenta, nor were they -- nor were they described or quantified in the embryos.

And most importantly, the authors did not indicate what the mode of exposure was supposed to be. And this is interesting, because those two substances have very low vapor pressures. This little table here indicates that compared to water, both of them are between

a million to several billion fold lower than water in terms of vapor pressure.

So there's really not much of it escaping into the atmosphere for breathing purposes. The photograph in the lower right-hand corner is a photograph of the caging that was used in these studies. And you'll notice that they have lids on them. The lids have some holes at the top or a hole in the top, in which a filter could be placed, but it's not a very large opening. And so the question remains how do we think the animals got exposed to the material?

I'd also call your attention to the fact that if you look at that cage, there are five mice in the cage. The cages are designed to hold five mice.

The next slide --

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DR. DeSESSO: -- we'll talk about the dose calculations. And in this case, recall that in toxicology experiments, dose is calculated as the massive material that gets into an animal on a daily basis or the milligrams per kilogram per day. And in this particular set of experiments, the authors did not weigh the female mice during gestation saying they didn't do that, because the weights were variable. And, of course, in mammals, they are variable and mice gain approximately 40 percent

more body weight during the course of gestation, which means that you need to adjust the dose as you go through gestation.

We don't know what they -- how that was done in this study. And the dietary material was applied to the animals by a gel cube that had incorporated in it the laboratory cleaning solution. And these gel cubes were then placed in the cages on an as-needed basis. But the authors don't really tell you how they monitor how much the animals ate. A typical mouse in early gestation weighs between 30 and maybe 32 grams. It gets up to be as high as perhaps 35 or 38 by the end of gestation. So these cubes were pretty much the size -- 80 percent the size of an animal.

The authors stated that the animals consumed 28 percent of their weight per day. And it's not clear how that was measured, because they didn't weigh the animals. And we don't what -- how they figured out how they -- how much of the cube they ate, unless they weighed it before and after, but there were no records of that.

And importantly, they didn't -- they weren't clear as to how many animals there were in each cage, and so if you had five mice in the cage, then you've got another variable there. And some animals might eat more than others or some cages might only have four animals in

it.

So it appears to us that the doses were based on a series of estimates and not really on measurements.

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DR. DeSESSO: And so the last thing I wanted to talk about, with respect to this, was the use of the word -- of the term neural tube defects. And you have to understand that neural tube defects are really a loosely defined sted of mal -- set of malformations that are seen at term.

In humans, of course, that's after birth. In a mouse that would be somewhere around day 18 or 19, because gestation usually lasts about 20 days. These defects -- neural tube defects, always affect the coverings around the -- around the central nervous system. That's the meninges that surround the brain, and the spinal cord, and the skull -- or the vertebrae, which protects those. They may or may not involve malformations of the brain and spinal cord itself.

And so that's an important -- an important difference between what was described here and what was -- what we would see in a day ten and a half mouse embryo.

On the next slide --

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DR. DeSESSO: -- we want to -- we want to point out that these slides -- these embryos were identified and looked at on gestational day 10.5. The gestation period of a mouse is about 20 days. And the neural tube is a structure that basically forms something like rolling up a newspaper and then eventually the two ends have to be folded together at the cranial end and at the caudal end.

And then that cranial end closes at about -- late on day nine or early on day ten, which is just shortly before the time these authors look at the -- at their embryos. And at that period of time, the meninges and the skull have not been formed and they won't form for another four or five days, so they could not be affected.

The photographs that they published show embryos, several of which, especially treated embryos, are at a younger gestational stage than are the controls. And this indicates to us it's probably a case of developmental delay. And it is reinforced by the fact that when they did allow pregnancies to go to term, in none of their papers did they describe any neural tube defects in the offspring.

So this suggests that the findings either were developmental delays or they may have been findings related to animals or embryos that were dying, which is called a resorption. And resorptions occur quite commonly

in rodents, because rodents have anywhere from 14 to 20 embryos at one time. They don't all make it through gestation.

The next slide, please.

--o0o--

DR. DeSESSO: Now, in terms of the other studies, our interim results looked at those other studies, the four in the category -- in the reliable and the two in the reliable with restrictions. And it's interesting that in none of those studies did we see any neural tube defects or any other malformations at doses as high as 200 milligrams per kilogram per day.

Interestingly, the United States Environmental Protection Agency and the European Chemicals Agency have approved both ADBAC and DDAC. And when you look at their assessments, they're based on studies, all of which are in that dose category in one -- in category two studies as we had talked about.

The most recent of those was the one performed by ECHA, which occurred in 2020. And that specifically considered and rejected data from those studies in category three. And there's a statement here that they made that the QACs could be used -- those QACs could be used as disinfectants in animal facilities, as long as they're used following directions.

So at this point in the analysis, the working group concurs with the regulatory agencies.

Next slide, please.

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DR. DeSESSO: The conclusions -- the interim conclusions of our systematic review, at this point, are that the data that we've reviewed in the categories one and two indicate that it's a rather robust and extensive set of data. We're working through other data. We're hoping to get some more data from Europe to add to this, looking at both the published and unpublished studies.

But at this point, we would be saying -- we would be concluding that neither of those chemicals are developmental nor are they reproductive toxicants, and thus, we are -- our conclusions align with those of EPA and ECHA. And it is our intention to publish this assessment once we're finished with it.

The next slide.

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DR. HOSTETLER: The next slide is back to me. Thank you for that, John. And just to wrap-up the conclusion that QAC -- disinfecting QACs do play an important role in protecting human health. They control a wide variety of disease-causing organisms, effective at low concentrations.

And I really want to point out that guidance and concerns about use, and overuse, and frequent use, the CDC guidelines and EPA's websites on the proper use of disinfectant chemistries is really quite extensive and really quite complete, and offers specific directions on safe use. And I think that's an important consideration.

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DR. HOSTETLER: And that's the end of our presentation.

CHAIRPERSON SCHWARZMAN: Thank you very much to both of you. We have 15 minutes now for questions from -- and comments from both panelists and audience members. And panelists can ask questions by just raising your hand. I don't see everybody yet.

Oliver has a question to start us off.

PANEL MEMBER FIEHN: If none of these compounds are volatile, how can it -- can it be that it has been measured in air?

DR. HOSTETLER: You're referring to Dr. Salamova's paper --

PANEL MEMBER FIEHN: Yes, that is just what we heard today. I'm referring to what I heard today --

DR. HOSTETLER: From my --

PANEL MEMBER FIEHN: -- (inaudible) and they were clearly detected at levels in air.

DR. HOSTETLER: My understanding was she sampled for three weeks at a time before getting detectable levels, is my understanding. Maybe I misunderstood.

PANEL MEMBER FIEHN: No. She just -- okay. So on the one hand, I hear that you argue that there's no data and on the other hand, you say there's no need for data because everything is safe, and because it is not volatile. Now, what I've seen today is, A, it has been shown unequivocally now, in two presentations today, that it's being absorbed and regularly detected in humans all the time in blood and in other biofluids, and B, that it has been detected in air by passive sampling.

Now, these are two things I did not know before coming into the meeting, where I think these are in conflict to, you know, what we heard before. And that's, you know, based on published data before, but that's the idea of science, and that's also the idea of, you know, going forward is to acquire data that may be, you know, giving us more insights.

DR. DeSESSO: Well, I think there's a possible -- am I on? Can you hear me?

DR. HOSTETLER: Yeah, you're on, John.

DR. DeSESSO: Okay. Yeah, I think one of the things that could happen is that it's a possibility that materials could be used and spritzed and allow aerosols to

form. And the aerosols might be a vehicle by way of which some of this could get into the -- into the animals.

But in terms of the way these disinfectants are used and according to the directions, these -- you know, LabSand is one of the substances they use. It's to be used and left on the material on the hard surface and left alone, because that's how it's worked -- this antimicrobial work. At that point, there should be very little --

PANEL MEMBER FIEHN: So you say that these products are never sprayed --

DR. DeSESSO: Yeah, they -- pardon me?

PANEL MEMBER FIEHN: So they should not be allowed to be sprayed in a spray?

DR. DeSESSO: No. There's the animal -- there's the animal one.

PANEL MEMBER FIEHN: And that the spray means generating aerosols, right? Is that correct?

DR. DeSESSO: You're saying --

DR. HOSTETLER: Yeah, let me comment on that, John.

Dr. Fiehn, you're exactly correct. They're approved for use in sprays. Typically, those pump sprays have coarse particle sizes that are not inhalable.

PANEL MEMBER FIEHN: So they are in the air, but

cannot be inhaled?

DR. HOSTETLER: -- (inaudible) more than 50 or a hundred nanometers cannot get into --

DR. DeSESSO: They're not respirable.

PANEL MEMBER FIEHN: So they are sprayed in aerosols, but they cannot be inhaled.

DR. HOSTETLER: They're typically, if they're high enough particles, they're trapped in the upper respiratory tract. They don't get to the lungs.

DR. DeSESSO: And then they -- and then they dissolve --

PANEL MEMBER FIEHN: So when they are either through dust or in the air, and we are exposed, so then we should not see it in the blood, is that correct? Is that the understanding now? So how --

DR. HOSTETLER: No, I'm saying that --

PANEL MEMBER FIEHN: -- come where we have two different reports today that unequivocally been shown to be detected in very frequent in the human population, when there's, you know, not supposed to be in contact normally.

DR. HOSTETLER: We're not saying that there's zero exposure. Nothing in my presentation said anything about zero exposure. My presentation said that when exposures in animals identify safe levels, in estimates of human exposure, which can occur, through dietary exposure,

through hand to mouth, result in potential exposures that are below levels that should cause concern.

Ten nanomolar in plasma that may be bound to plasma proteins, I would be interested to know what toxic endpoint is being driven by a ten nanomolar concentration of a quaternary ammonium compound.

PANEL MEMBER FIEHN: So we have data showing that these can be incorporated into mitochondrial membranes and disrupting the mitochondrial electron transport chain. So that's data from UC Davis that we have not published yet, but that would be a way how things can be harmful. So, you know, we're not saying -- this is not a discussion here about disallowing any use. It's about, you know, do we want to know more. That's, I think, what our California EPA is doing here, and why we are discussing this.

And with that, I'm shutting up.

DR. HOSTETLER: We're not telling you that you shouldn't be monitoring. We're telling you that what's the safety data when we know humans are exposed at low concentrations of what the data sets tells us. That is the --

PANEL MEMBER FIEHN: No, no, no, no. You said you have -- you have animal data. You have reviewed animal data, not human data. That's a different thing,

because before we also heard that rats are not humans and that rats have a quite different turnover than humans. And I'm sorry, you know, we don't have data on humans.

CHAIRPERSON SCHWARZMAN: I would add just one final point to this discussion of particle size, since there's a question of exposure here, is to return to my point about foggers, that sprays, as Keith said or was it John, I'm not sure, you know, produce similar from like 40 to 60, I think micron size particles. But foggers, I've seen evidence about one to ten microns and those are surely respirable, so --

DR. HOSTETLER: I believe everyone using foggers have -- are directed to use personal protective equipment.

CHAIRPERSON SCHWARZMAN: But what does that say about the air that remains in place and -- in terms of people who come through subsequently and all of that. So I just think that's a -- as long as we're talking about spraying, we should make sure we're covering all of the particle sizes that can be produced.

Other questions?

Tom.

PANEL MEMBER McKONE: Yeah. I just -- so I want to kind of go back to the point that came up at the end, which is, you know, the -- you reviewed a lot of studies and scored them, and focused on the, I forgot how many,

the ones that scored low and the -- that suggested a premise of -- or a hypothesis of toxicity. And then you worked very effectively to at least provide evidence to refute those studies. And then went to the other studies that suggested safety, and made the argument, well, those are robust and good.

But what concerns me in public health, we always work the other way around. We don't really start with a hypothesis that everything is safe or work against it. We really want to try to refute the hypothesis of safety, right? We want that to be the robust finding. And I guess what concerns me is the hypothesis or the statement we're working toward is safety for humans. And I don't think you can have a robust conclusion that something is high competence of safety for humans, if there's no human data.

The reverse of that is that if something is toxic to animals, it isn't necessarily true that it's toxic to humans, but it means that you're less comfortable making the assumption or operating on that premise, right? We always err on the side of trying to refute safety where it makes sense. So I think, you know, what we're stuck with still is the absence of human data. We're still stuck with that. I mean, we're stuck with the problem we would have if it were toxic in animals, but no human data, we

would say, well, it -- I mean, there's a lot of substances that are toxic to animals, but they're not toxic to humans, but we kind of start with that premise.

The other way around is something that's safe for animals is not always necessarily safe for humans. We might move with that as a working hypothesis, but would always struggle to learn more about it and not be happy with a very small number of studies in a few animals that seem to be good studies, but could always tomorrow be refuted by the study that isn't true, especially when there's some poorly done studies that suggest that the operating hypothesis is wrong. Sorry, if it was a bit winded, but that's kind of -- I'm a little concerned that this is (inaudible) --

DR. HOSTETLER: I don't know if there was a question or not exactly, but I would say this. The requirements that regulatory agencies, U.S. EPA, and ECHA, and others around the world make a very high bar for what data has to be conducted in order for them to evaluate that data and make a judgment on human risk assessment.

And that's what -- that's -- we're not asked to go out and test in humans. Some of the exposure data that this industry has paid for has been done in humans. There have been human exposure studies that pass human HSRBs. That data is publicly available.

So we're not trying to dodge. We're not trying to say that there isn't exposure. We're saying that we agree with the regulatory authorities' opinions, based on sound risk assessment properties that based on the data that exists, these substances are safe for use as directed.

PANEL MEMBER McKONE: Right. A lot of these agencies have made mistakes in the past. So, I mean -- I mean, the other question I have is we're asked -- we're looking at a class of 800 chemicals, and the studies that you're talking about are for a couple that are in use as disinfectants, so I think they're a bit different. And I -- even if we were fully at good data for safety of two or three compounds, I don't know if it says enough about a class of 800.

CHAIRPERSON SCHWARZMAN: I want to offer Amina the chance to address a question that was raised about her work. And then, Libin, I see that you're here.

DR. SALAMOVA: Yes. Thank you. It's a comment on the first question about inhalation and the air concentrations. Yes, we did deploy the air samples for three weeks, but that's a standard -- four weeks actually, but that's a standard procedure for indoor air sampling using PUF samplers. And we do it for other compound groups as well and we never see these high levels

actually. These were probably among the highest levels for indoor contaminants that we've seen in our analysis. And we usually -- we work with different chemical groups, including different types of flame retardants, PCBs, pesticides, et cetera. So that's a comment on the inhalation. So some of these compounds are volatile, especially ATMACs, because they also have lower octanol-air partition coefficients.

And in regard to that, I did not present the data, but we do have some preliminary data also in outdoor air. And those samples were actually collected using the high-volume samplers around for just one day. And in those sampling, we are able to differentiate between particle phase and vapor phase contaminants. And again, we see an interesting pattern, where we see higher levels of more volatile ATMACs in vapor phase collected with XAD absorbence and higher levels of BACs in particle phase collected with filters.

The levels for outdoor air are lower than for indoor air, but that's a trend we see for almost all contaminants that we work with. But again, the levels are higher than for the more known contaminants, like again flame retardants, PCBs, and some pesticides. So just wanted to comment on the air data.

CHAIRPERSON SCHWARZMAN: Thank you. We just --

have just a couple minutes left, Libin, if you have something quick.

DR. XU: So quickly, I want to -- one thing to clarify on the neural tube defects study, I read those papers. The ambient exposure is basically the facility using the QACs disinfectants. It doesn't necessarily they're applying directly on the cage, but it could be exposed through air, through, you know, animal facility; you know, working people. I think there are routes they can be again exposed to those compounds, because they exist in a facility.

So another comment I want to have is that I do not agree that all the federal agencies think they are safe. In fact, FDA, a few years back, has actually called for additional safety data for anti-septic over-the-counter products. Here's their language. I'm looking from their announcement in 2016. This says, "Since the FDA began review of topical antiseptic in 1970s, many things have changed, including the frequency of use of some of these products, new technology that can detect them, and FDA safety standards, and significant knowledge about impact of widespread antiseptic usage. And FDA is particularly interested in gathering additional data on the long-term safety of daily repeated exposure to these ingredients by consumers and on the use of these

products by certain population, including pregnant women and children, and for which topical absorption of active ingredients may be important".

So I just want to clarify this concept, because, you know, even though in older documents, by, you know, EPA, that was can be traced back 2006. But I think federal agencies now, you know, becoming more aware of the additional data that's needed for these kind of compounds.

CHAIRPERSON SCHWARZMAN: Thank you.

We need to move on now, but I want anyone who has additional questions or comments, we have significant time for discussion and please do keep those and I can get to you first in the -- when it's -- when it's next time for discussion. I see Veena had it -- a question and I will also check in -- Jenny also. So I will put you on a list and then I will also check in with Elizabeth, if there was anyone else waiting to speak. So we'll have plenty of chance to get to your comments. Please do remember them.

Thank you very much to our presenters, John and Keith, for your presentation. And we're going to move on to our final session of the day, that is considering QACs as potential priority chemicals. I want to reintroduce Shoba Iyer, who's our staff toxicologist in the Safer Alternatives Assessment and Biomonitoring Section in OEHHA. Shoba will present OEHHA's document on QACs as

potential priority chemicals for Biomonitoring California and she'll outline the options for the Panel. And then we'll have a chance for questions, a chance -- Panel questions, that is, a chance for public comment and then the Panel will deliberate.

So I'll turn it over to you Shoba.

(Thereupon a slide presentation.)

DR. IYER: Great. Thank you, Meg. Can you just confirm for me that you can see my slides in full-screen mode again?

CHAIRPERSON SCHWARZMAN: Yes, all is good.

DR. IYER: Great. Thank you.

Okay. My presentation now will be an overview of OEHHA's potential priority chemicals document on QACs, as well as other information relevant to the criteria for potential priority chemicals.

The potential priority chemicals document builds on OEHHA's 2020 potential designated chemicals document and OEHHA's 2019 preliminary screening document on QACs. The PDFs of all three of these documents are posted on the Biomonitoring California website on the page for today's meeting.

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DR. IYER: Here, I'm showing you again the criteria for recommending priority chemicals. The SGP can

recommend priority chemicals for biomonitoring in California from the list of designated chemicals.

These criteria are: the degree of potential exposure; the likelihood of a chemical being a carcinogen or toxicant; the limits of laboratory detection; and other criteria that the Panel may agree to. And I'll remind you once more that these criteria are not joined by the term "and", and the Panel is not required to specify other criteria.

Now, we heard about limits of laboratory detection for selected QACs in Libin's and Amina's presentations today. So in this presentation, I'll cover some information relevant to the first two criteria shown here.

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DR. IYER: There is significant potential for exposure to QACs. I'll cover some relevant highlights on this slide. Of the QACs I reviewed, the national production volume for 20 of them was over 100,000 pounds in 2015. Of these, 11 had production volume of over one million pounds.

QACs are used in a wide variety of applications, including as antimicrobials and disinfectants, as we've heard. Approximately, 46 percent of the disinfectants for coronavirus on U.S. EPA's List N include QAC active

ingredients.

Detections have been reported in indoor air and dust samples. And we heard about these recent findings an in Amina's presentation earlier today. QACs have been detected in other environmental media, including sediment, sludge, and wastewater treatment plant influent and effluent. And we heard about environmental detections in Bill's presentation this morning, including in sediment samples collected from the San Francisco Bay.

According to a summary of market research available online, the global QAC's market is forecasted to grow by over 60 percent from 2019 to 2027.

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DR. IYER: There are possible health concerns associated with members of this chemical class. I'll cover some highlights here. And most of this information is drawn from OEHHA's 2020 potential designated chemicals document.

Some QACs are linked with dermal irritation. One example is quaternium 15, which is used as a biocide, preservative, and surfactant in cosmetics and personal care products and in cleaning products. It's a formaldehyde-releasing preservative. Some QACs are linked with respiratory effects. The Association of Occupational and Environmental Clinics has identified some BACs, and

one DADMAC as asthmagens, which they define as a substance known to cause asthma, which is acquired de novo from a workplace exposure.

Studies conducted among hospital staff, such as nurses and housekeeping staff, have reported that exposure to QAC-containing disinfectants and cleaning products can be linked with work-related asthma. This topic was covered at the SGP meeting in March 2020. And in today's meeting, we've had some discussions about a potential for increased exposure to these subpopulations.

In addition, respiratory effects, such as pulmonary inflammation, have been observed in studies of rodents exposed to QACs. Diquat dibromide and paraquat dichloride are quaternary ammonium herbicides and exposures to these QACs have been implicated in neurodegenerative diseases, such as Parkinson's disease.

In rodents exposed to some QACs, reproductive and developmental effects, such as decreased fertility and neural tube defects have been reported. We heard a presentation on this topic from Terry Hrubec of the Edward Via College of Osteopathic Medicine in Virginia at the March 2020 SGP meeting. Other literature on this topic was summarized and/or cited in the potential designated and potential priority chemical documents.

Some immunological effects have been reported in

in vivo studies, such as alterations in immune response genes and in antibody production in mice exposed to some QACs. Altered cellular function, such as inhibition of mitochondrial respiration has been reported in in vitro studies of some QACs. And I'll note that plasma membrane disruption is the general mechanism of action that makes QACs effective as preservatives, disinfectants, and biocides. So it makes sense that the mitochondrial membrane can also be impacted.

In vitro studies of benzalkonium chlorides have found inhibition of cholesterol biosynthesis and altered lipid homeostasis. And we heard about some of this research in Libin Xu's presentation at the March 2020 SGP meeting.

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DR. IYER: There are some publications about the potential for antimicrobial resistance to QACs. Shown here are screenshots of some of the work that's been published on this topic within the last year. We included these publications in the references list of the potential priority chemicals document. And we touched on this topic in the potential designated chemicals document.

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DR. IYER: Here again are the Panel's options following their deliberations this afternoon. The Panel

can recommend the class quaternary ammonium compounds or QACs be added to the list of priority chemicals, defer consideration of QACs, or decide against adding QACs as priority chemicals.

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DR. IYER: And I'm happy to take questions at this time.

CHAIRPERSON SCHWARZMAN: Thank you so much, Shoba. Sorry, finding all the appropriate buttons.

DR. IYER: Same here.

CHAIRPERSON SCHWARZMAN: We have time for -- we have just a few minutes here for clarifying questions only from the Panel. And we'll have substantive -- time for substantive discussion. So clarifying questions for Shoba only now, please?

Anything about the process of designating or considering these chemicals as priority?

Carl.

PANEL MEMBER CRANOR: I'd just like clarification on the listing as a priority chemical. I take it that that does not commit anybody to do anything, but it opens up the possibility of biomonitoring in case problems are seen. So in some sense, this is not a -- I don't want to understate it. It's not a particularly threatening thing. It just gives the Biomonitoring Committee, and maybe some

other agencies, the possibilities of doing something with it if the data turns out. Is that -- is that on -- is that correct?

DR. IYER: Well, the Panel recommended that QACs be added to the list of designated chemicals last March, which means that they could be biomonitored in a Biomonitoring California study from being on that list.

Here the Panel has an opportunity to discuss recommending QACs as priority chemicals for biomonitoring.

PANEL MEMBER CRANOR: Thank you.

CHAIRPERSON SCHWARZMAN: We actually do have a couple more minutes, because Shoba was quick. So, Tom, go ahead.

PANEL MEMBER McKONE: Well, I just want to add to -- to our -- as I recall from previous discussions, we wanted the option to make these priority compounds, because we got so much information on the rapidly increasing volume of production and use in our previous meeting. So that was one of the issues that motivated not letting them just sit in the background as compounds that could be brought forward at some point, but that there was sufficient evidence of rising use that it would be a good time -- it would be a priority, because this is similar to what we did to other classes of compounds, like the cyclic siloxanes, where we said, oh, we want to get on top of

things when the -- when the production levels are rising, not after they peak, and then we start seeing them show up at levels that are a bit surprising.

CHAIRPERSON SCHWARZMAN: Any other questions for Shoba?

If there's no further questions, then we can open to public comment. We have about 15 minutes for public comment. And I'll just go straight to Elizabeth to see if there's anything submitted by email or by the GoToMeeting webinar interface.

DR. MARDER: There are no questions and no requests to speak at this time on Shoba's presentation.

CHAIRPERSON SCHWARZMAN: Maybe I could just get clarification from Sara. This is -- there's an open public comment that occurs after -- at the end of the day. But Sara was this public comment meant to be restricted to Shoba's presentation?

MS. HOOVER: No. This is not --

CHAIRPERSON SCHWARZMAN: Yeah. My understanding is --

Okay. Thank you. Sorry to interrupt. My understanding was this was meant to be more general.

MS. HOOVER: That's right. This is public comment on QACs as potential priority chemicals generally. So it's the public's opportunity to comment on anything

they heard earlier, anything they want the Panel to hear before you guys discuss your recommendation. Also, depending on how much time you use in your discussion, the public could still potentially chime in during that discussion. But basically now is the opportunity, if anybody, either speakers, or the audience, or people listening from afar want to chime in, this is the time to do it.

DR. MARDER: And we do have that unanswered comment from the last session, Sara, if I made read it now, while we're waiting for other --

MS. HOOVER: Sure. Yeah. I think it's already -- I think we decided it was already covered, but -- if I'm not mistaken, but go ahead.

DR. MARDER: Okay. Well, this was related to a question that was answered, and I think maybe it was fully answered. By Emily Bryson from DPR asked, in the -- and following up to the discussion that was the brief discussion Meg had about the QACs being applied via foggers, how would the use of a fogger affect the particle size and inhalation potential? And so that may have been sufficiently addressed, but that was the last remaining question we had.

CHAIRPERSON SCHWARZMAN: Thank you for raising that. Just because I said it, I'll sort of mention again

that the literature that I saw was that where sprayers can produce -- tend to produce larger particle sizes like 40 to 60 microns, that fogging tends to produce particles that are one to ten microns, which are, you know, in the respirable range. But I would also welcome anybody else weighing in on that point, since it's just my looking at the literature not having done that work myself.

If there are speakers from other points -- parts of the day who have done that related exposure work and want to weigh in.

Otherwise, let's see if there's any additional public comments which is open now for, as Sara said, any topic from the day that you want the Program or the Panel to hear before our deliberations and vote on the -- whether to recommend prioritizing QACs.

I'll also just mention that Biomonitoring California received three written public comments last week. Those have been circulated to SGP members and they're also posted on the meeting page for this meeting. One was from the ADBAC Issues Steering Committee, which submitted comments regarding the use of analytical methodology for measuring antimicrobial QACs in environmental and biomonitoring samples.

And there were two comments from Women's Voices for the Earth. One was about some special vulnerable

populations that may have excessive exposures to QACs during COVID-19 and beyond. And the other was comments on the U.S. FDA's review of ADBAC and the identification of data gaps in the body of scientific literature on the safety of QACs. And I think that was actually referenced by the Libin earlier.

So just to highlight that those comments were received by the Panel and they're also posted for public viewing on the website for today's meeting.

Elizabeth, any other --

DR. MARDER: We have --

CHAIRPERSON SCHWARZMAN: -- public comments.

DR. MARDER: We have no public comments via email or via GoToWebinar at this time and we have no requests to speak at this time.

CHAIRPERSON SCHWARZMAN: In that case, I would suggest that we proceed to Panel deliberation and recommendation. And I want to turn first to the Panelists who were -- had something to say earlier that we didn't have time for, and that's first Veena and then Jenny.

PANEL MEMBER SINGLA: Thank you. And Shoba actually mentioned this in her presentation as well. You know, in a previous discussion, several folks spoke about the lack of human data. And I had just wanted to comment on the strong evidence we do have on QACs and work-related

asthma, as one very relevant data set there.

CHAIRPERSON SCHWARZMAN: Great. Thank you, Jenny.

PANEL MEMBER QUINTANA: Can you hear me?

CHAIRPERSON SCHWARZMAN: (Nods head.)

PANEL MEMBER QUINTANA: Great. I'd like to thank the speakers for all the literature they -- review that they did on these compounds. And I had a couple questions about the toxicology and risk assessment presentation, just a couple clarifying questions.

One was the study in the animal cages where they're using the compounds for like ambient cleaning in the room. What was the birth -- what was the endpoint? I don't believe it was on the slide. I went back and looked. What was the reproductive endpoint for that study? Was it also neural tube effects or what was the reproductive endpoint that they claimed in this study? That was one question.

And I'll ask my second question too, if you're going back to the slides.

Sorry, go ahead?

DR. HOSTETLER: Can I answer that question?

(Multiple voices at once.)

DR. HOSTETLER: Or I don't know if John is still on or not.

DR. DeSESSO: Yeah, I'm still here.

DR. HOSTETLER: That specific viewpoint was the publication that was titled Ambient Exposure Causes Neural Tube Defects. So the endpoint was, in fact, neural tube defects, which was -- using that term correctly was incorrect.

PANEL MEMBER QUINTANA: So there was no other reproductive endpoint that was assessed in that study in the animal cages? I just want to make sure I'm clear about that.

DR. HOSTETLER: John -- I don't know if John is still on or not. John (inaudible) --

DR. DeSESSO: Can you hear me?

DR. HOSTETLER: Yeah.

DR. DeSESSO: Okay. So the -- there were some -- the data showed an increase in resorptions in the highest dose, which was 120 milligrams per kilogram, according to what their calculations were. The -- it's -- they were -- I think they were -- I think they were -- if I recall, they were around 12 percent and the controls were something like around six percent so they weren't -- it wasn't dramatically increased, but it was increased.

PANEL MEMBER QUINTANA: Thank you. And then the other question was you were saying for ingestion -- or for exposure to a toddler. And I just wanted to clarify, was

that done on ingestion of dust only, rather than any dermal or inhalation component? As some kind of more recent assessment of risks from dust have looked at exposures to the dust by ingestion, but also by the suspension of particles, and inhalation, and dermal exposure and I'm just -- and partitioning into air. And I'm just curious if that was based on ingestion of dust.

DR. HOSTETLER: In my slide where I reference Dr. Salamova's work, that was directly from her paper, which talked about dust ingestions and calculated exposure in toddlers on a milligram per kilogram basis. I do refer you to the workplan with EPA where they'd look at all kinds of age groups and potential indirect exposure from indirect food contact, and therefore dietary exposure. And those have EPA's conservative modeling in what those dietary ingestions exposures are estimated to be.

PANEL MEMBER QUINTANA: Thanks. My last question was, I know you reviewed a lot of literature. Did you come across any effects on the microbiome of animals?

DR. HOSTETLER: There's some of the chronic studies where animals were fed for their entire life, particularly in dog studies, because their microbiome was wiped out, then they got gastrointestinal distress and diarrhea from that. And that's not unexpected from an antimicrobial being given orally.

PANEL MEMBER QUINTANA: Okay. Thank you very much for clarifying that.

DR. HOSTETLER: You're welcome.

CHAIRPERSON SCHWARZMAN: Libin.

DR. XU: So I want to respond to Jenny's question on the -- I guess the study by Terry Hrubec on the neural tube and also some of the earlier study actually on the reproduction. So I think in 2014, they published a paper where the study carried on like a six-month breeding study, like with exposure to QAC. They found decreased reproduction, decreased fertility, and fecundity of -- in mice. So that was before the neural tube study. I think the neural tube study like was a few years later. They looked at neural tube defects.

And I think it's -- or the other presenter also mentioned even if there's no neural tube defects, there -- at the later time point, but there's neural tube development delay, right? So there's -- apparently, there's that difference happening there.

So -- and another thing, you also asked about a microbiome. We did a study to look at those. I think my student has presented it at a couple of occasions. We do see some alteration in microbiome. Exactly how does that affect say in the -- over a longer term human health, we don't know yet, but the microbiome were changed with

exposure. Yeah, that's from one of the study where we actually analyzed the QACs and their metabolites in the feces. Yep.

DR. HOSTETLER: Megan, there was -- if I could, there was a point where Libin was talking about the FDA's call for more data and I was going respond to that just when the comment period ended. So is it appropriate, can I make a comment on the FDA's request for more data?

CHAIRPERSON SCHWARZMAN: Sure. If that was intended as public comment, and then we'll move on to panel deliberation.

DR. HOSTETLER: Certainly public comment. FDA has, in fact, had quaternary ammonium compounds as antiseptic uses approved for over-the-counter use since the 1970s. QACs fall in a really unique position in that they were recommended by FDA along with isopropanol and ethanol during the pandemic, because of the public health crisis of people needing to sanitize their hands.

FDA has asked for new uses. These are new uses. They have asked for more data. There are -- the industry is cooperating and they've actually done some exaggerated hand wash studies 30 times a day for 30 seconds and looked at with what happens. And at the moment, preliminary data suggestions concentrations are below any levels that the Center for Evaluation of -- Center for Drug Evaluation has

no concerns with the current data that's in hand. It's being evaluated. It's a new use. FDA evaluates the new uses differently than EPA, so that work is ongoing.

CHAIRPERSON SCHWARZMAN: Thank you for that. I would note as a physician, I can say that 30 times of hand washing a day is not exaggerated. If you're washing your hands before and after each patient and before and after meals and all of that, that is certainly not outside the realm of what you do on a daily basis.

DR. HOSTETLER: So noted.

CHAIRPERSON SCHWARZMAN: Just in terms of terming that study.

All right. Thank you all for your contributions. I just -- as we move into the Panel deliberation, one note is that José Suárez won't be voting on this item, because he had to miss some parts of the presentations on QACs, but he will still participate in the discussion.

So I want to open it up to Panel members to discuss your thoughts and input to the Program on the potential to designate QACs as potential priority chemicals, if anyone wants to start us off.

Go ahead, Veena.

PANEL MEMBER SINGLA: From my perspective, I think the QACs do meet several of the criteria for consideration as priority chemicals. The degree of

potential exposures we heard about today, some concerning data on widespread exposures there, and on toxicity. As well, we heard about in a previous Panel meeting, the work-related asthma data, as well as the emerging concerns on the reproductive and developmental toxicity.

CHAIRPERSON SCHWARZMAN: Thank you.

Jenny.

PANEL MEMBER QUINTANA: Hi. I much agree with what Dr. Singla said and also to say that we started out today by talking about focus for our biomonitoring efforts in vulnerable populations and special populations in California were among those. And I think the -- to me, the potential for occupational exposures, especially among some of the most vulnerable workers, such as cleaners, makes it like a very compelling story to me on top of the other considerations. And I don't see the use going down any time soon. I -- with the need to maintain safety in new variants coming up, I just feel the potential for exposure perhaps is only going to increase, as people get out and about more to cleaned environments.

CHAIRPERSON SCHWARZMAN: I had -- Carl, I'll get you next -- just a similar thought to add on to what Jenny just said, that I see a lot of overlap between the people who are considered essential workers during the pandemic, and those who are potentially more highly exposed because

of increased disinfection use. And not only -- not just because they're -- I mean, it's partly because they're out there working in settings that require, or at least are recommended, to have increased disinfectant use.

And I agree with Jenny that, you know, we could see this as a very temporary spike. And I think that's less likely than -- that some of these practices, or to some degree, they will become the norm, especially when you see what happens to -- sort of we're seeing what happens to influenza cases and influenza deaths as a result of all of the, you know, masking, and distancing, and potentially also disinfecting practices that we've adopted during the pandemic. And it's reasonable to conclude that some of those practices would be recommended to continue, even in the hopeful event that we could get the current pandemic under better control. So just to add to what Jenny was contributing.

Carl.

PANEL MEMBER CRANOR: Yeah. Yes. Thank you. I agree with Jenny and Megan. And I appreciated Tom's comment earlier about staying ahead of the curve, because we know that there are a lot of unfortunate substitutions that occur. And it's very difficult for public health protections to keep up with the rapidity with which new chemical substances are created and used for similar

purposes, and nobody has any idea how safe they are. And so it seems to me that all of this is an argument for making it a priority chemical.

CHAIRPERSON SCHWARZMAN: Tom and then Eunha.

PANEL MEMBER McKONE: So I summarized it. I'm inclined to, you know, agree, but state this a little differently. I think, you know, with regard to exposure and evidence of widespread exposure, I think the information we saw is significant and compelling for our case. I think in terms of the ability to biomonitor what we've seen is compelling -- you know, more than sufficient and compelling to go forward. And the only thing we might say that although the toxicity may be incomplete and not compelling, it is at a point where there are enough issues of concern to warrant action now.

And it's kind of, you know, what Carl said about my point earlier, and to extend that is when there is evidence of concern -- or sufficient evidence to raise concern, then it's in the best interest of public health to collect the data we need to understand that better.

And that's one of the things we can do by making this a priority chemical. We will learn more, especially about highly exposed groups. And we will learn more to be able to sort them out and to see who's showing symptoms or not showing symptoms.

But it's not the time to say, well, the evidence is not sufficiently compelling to declare this toxic. Well, the evidence is sufficiently compelling to say we could have a problem for us to move forward on the tools to understand the nature of that problem.

CHAIRPERSON SCHWARZMAN: Eunha.

PANEL MEMBER HOH: I definitely agree with all the previous Panel members' opinions. I think how we have plenty of examples of chemicals that, you know, it came to so late, once it so spread out in the environment, and then so many exposures are happened already. And then this -- you know, we wait too long and it's so hard to remediate, and clean up, and anything like that afterwards, or even we completely ignore it, you know, the high exposure groups.

I think it's very important time and it's critical. Because the public's understanding the use of disinfectants, because of COVID-19, it's going to be -- it's not going to disappear. It's going to be increasing and increasing, especially for the very young age children's exposure. It's going to be more -- it seems like more concerning, not only those occupational high-exposure groups. So I think it's very important to show the evidence. And a lot of environmental fates and what we observe and based on, you know, I mean, it's

convenient and also it's very important, based on the chemical properties, and physical properties, you know, that could predict, you know, how those chemicals behave.

But a lot of times, the chemicals have a lot more -- their behavior is a lot more complex. So we cannot -- there is so many examples that we say, like, oh, these chemicals are not going to be persistent. These chemicals are not going to be in the air. There's so many examples we went through. But in the end, they were absolutely in the air. They're absolutely, you know, persistent. So I think it's a very important time to -- I think we have to include them. I mean, we have to consider them. Yep.

CHAIRPERSON SCHWARZMAN: José, please.

PANEL MEMBER SUÁREZ: Yeah. Thank you. Thank you for the time. Just to remind that I'm not going to be voting on this. Nonetheless, hear are my comments. While looking at the criteria for recommending priority chemicals that were listed there by Shoba, slide two and then earlier, it seems like for the limits of laboratory detection, we have ample evidence that these can be detected in blood, and stool, in urine. And so from that point, we have met that criteria.

That it would be for potential exposure, I think that's pretty obvious. That's been very well documented

today. And then likelihood of a chemical being a carcinogen or a toxicant, here is, you know, a little bit of the great part of it, in the sense that, the conclusion, at least based on my understanding, is that there is, to some extent, insufficient data, really to show how toxic these chemicals are. But that doesn't mean that they're -- the lack of data doesn't mean that they're safe. It just means that there's a lack of sufficient evidence for this.

So thinking of it more from a precautionary principle type, even though this is way past that point, right? These chemicals were released back in the 30s and 40s. We did reach -- I truly believe that we do need to understand what's happening with this piece, especially given the large potential exposure, and this very substantial increase in exposure that we've seen, especially this past year. And this is likely -- this increase in exposure is going to be probably steady, if not increasing over the next few years. So from that -- from those points of view, I would be more inclined -- even though I'm not voting, more inclined towards designating these as priority chemicals.

CHAIRPERSON SCHWARZMAN: Thank you for that José. You're, by all means, allowed to make whatever comments and contribute to the discussion as you like.

Oliver.

PANEL MEMBER FIEHN: Yes. So I was really intrigued today by seeing these two reports today that we have frequent detection of these chemicals in various human biomes. Before when we started this a year ago, it was said that, you know, the ideal -- the overwhelming confidence of people in the field was that these would not be -- not be absorbed. And this is refuted. So this is very clearly not the case, because we can see it in humans.

Now, we don't know the way of exposure. We don't know how they get into people, not for sure. There are multiple ways they could be done. But this is -- was not tested on people with high exposures. So those were on regular students and regular folks in households, not even on people with high exposures. So that clearly justifies that we need to be knowing about the population at large a priority, because also the concentrations that were measured were higher, sometimes a lot higher, than for other chemicals that we otherwise monitor, right?

At the same time, the chemical structure is made to be harmful to membranes. That's the idea, right? So the last time I checked, we have membranes. So I understand that nobody wants that these chemicals be eliminated from hospitals, right? Everybody understands

the direct health effect of pathogens and that we need to be able to have clean rooms, like in surgery in a hospital. Yeah, absolutely. You don't want, you know, infectious pathogens there. But that was the idea and not, you know, 30 times hand washing, with that material, and spraying, and residential areas.

And children cleaning classrooms, you know, that was not the idea of these chemicals. That's why not were -- you know, they were meant for.

And I -- you know, in order to have a risk-use balance assessment, we cannot just rely on data from rats, oral, you know, given, because we are not rats and our metabolism is different. And it may turn out that when we have lots of data that we see that in humans the turnover is so high, that the concentrations never reach high concentrations in tissues, in cells, in different organs. We may see that in ten years from now. But today, we don't have that data.

And I think for California seeing that high volume of these chemicals in various applications and with exposure to people at risk, I think it's necessary to have this as a priority chemical on the list for the state of California. And we can only hope that the EPA will listen to our argument.

CHAIRPERSON SCHWARZMAN: So I am getting a clear

sense that there's general agreement on the Panel. And so I wanted to call for a motion, if anybody would like to make it, on the prospect of designating QACs as potential priority chemicals.

Veena. So Veena --

PANEL MEMBER SINGLA: (Raised hand.)

CHAIRPERSON SCHWARZMAN: -- Dr. Singla then motions that the chemical class of quaternary ammonium compounds be included as priority chemicals for the Biomonitoring Program.

Do we have a second?

PANEL MEMBER CRANOR: Second.

PANEL MEMBER FIEHN: Second.

PANEL MEMBER McKONE: (Hand raised.)

CHAIRPERSON SCHWARZMAN: So Carl, I heard that one first, seconds the motion.

And then I'd just like to take a vote. I'll go through you as I see you on my screen and you can indicate whether you support or oppose.

Eunha?

PANEL MEMBER HOH: Yes.

PANEL MEMBER CRANOR: I'm sorry. What do you need, voice vote, or hands, or what?

CHAIRPERSON SCHWARZMAN: Carl, I took you as a second, so you're a voice vote already.

PANEL MEMBER CRANOR: Okay.

CHAIRPERSON SCHWARZMAN: And I'm -- I'll request a voice vote of each individual person. Thank you very much.

PANEL MEMBER CRANOR: Okay.

CHAIRPERSON SCHWARZMAN: So Eunha, I heard as a yes.

And Jenny?

PANEL MEMBER QUINTANA: I support.

CHAIRPERSON SCHWARZMAN: Tom?

PANEL MEMBER McKONE: Yes, I support.

CHAIRPERSON SCHWARZMAN: Great. And Oliver?

PANEL MEMBER FIEHN: Yes, I support.

CHAIRPERSON SCHWARZMAN: And I also support this motion. So that makes it a unanimous motion, among the voting members of the panel currently.

MS. HOOVER: Meg --

CHAIRPERSON SCHWARZMAN: Yes.

MS. HOOVER: -- just to clarify, Carl should still vote. You should still ask him for his vote. Seconding a motion, that's not his vote.

PANEL MEMBER CRANOR: I support.

CHAIRPERSON SCHWARZMAN: Thank you for that, Sara.

PANEL MEMBER CRANOR: Thanks, Sara.

CHAIRPERSON SCHWARZMAN: Thanks for clarifying.

And now I can say it's a unanimous recommendation of the Panel to include QACs as priority chemicals in the California Environmental Contaminant Biomonitoring Program. So with that, that concludes our deliberation and recommendations section.

And we have ten minutes designated for open public comment at this point. It's -- we'll accept comments on any topic related to Biomonitoring California. And I will turn to Elizabeth for -- to find out if we have anybody who wishes to speak, or has presented anything to the Program via email, or indicated they want to comment via GoToMeeting.

DR. MARDER: We do in fact have -- we don't have questions yet, but we do have a hand raised. May I go ahead and unmute?

CHAIRPERSON SCHWARZMAN: Have on one second, Elizabeth, because I see that Carl needs to say something.

PANEL MEMBER CRANOR: Yeah. Yes. Thank you. This is my second meeting for the day. And I have a third one that began a few minutes ago, so if you would excuse me, I will leave. Thank you.

CHAIRPERSON SCHWARZMAN: Great. Thank you. Thanks, Carl.

Elizabeth, thank you. You could go ahead.

DR. MARDER: Okay. Nancy Buermeyer would like to speak again and I'm unmuting your now, Nancy.

MS. BUERMEYER: Okay. Can folks hear me?

PANEL MEMBER McKONE: Yes.

MS. BUERMEYER: Great. Nancy Buermeyer, Breast Cancer Prevention Partners again. Unfortunately, I was not able to see most of today's schedule, but I did want to make a comment about the importance of what you're doing in putting chemicals on the priority list, and particularly classes of chemical on the priority list.

The California Biomonitoring priority list is part, as you know, of the DTSC Chemicals of Concern lists. And that list has been used in a number of pieces of legislation to get disclosure in product categories that we have not had disclosure in before, so cleaning products, the fragrance in flavors in personal care products, chemicals in menstrual products. And we're working on one now to try to get disclosure of chemicals in cookware.

So every time you put something on that priority list, even if the -- even if the Program doesn't have the resources to do the actual biomonitoring, it still makes a huge difference in being able to better understand where these chemicals are in consumer products. And so I really want to thank you for doing all the work that you do and

for continuing to add chemicals to this list. It's really important for the work that we do to try to advocate not only to know what's in these products, but to get them out of these products.

So thanks very much.

CHAIRPERSON SCHWARZMAN: Thank you for that comment.

Elizabeth, anyone else who would like to make a public comment?

DR. MARDER: We have no raised hands and no questions submitted at this time.

CHAIRPERSON SCHWARZMAN: Okay. Then Veena has something to add.

PANEL MEMBER SINGLA: Thank you, Meg. I just had a general comment or suggestion that I think it would be helpful for the Panel to ask all presenters to disclose funding sources for work presented to the Panel and make explicit conflicts of interest disclosure statements. I think it's -- those are very helpful in being able to evaluate any of the work presented to the Panel.

CHAIRPERSON SCHWARZMAN: I second that suggestion. And I just want to ask Sara, if there is a general sort of protocol that's provided to presenters in those lines? I know some people just take that practice when they're presenting their research is presenting the

funding that they received for that research, but is anybody given guidance about it?

MS. HOOVER: No. Actually, I think that's a great point. And I think Kristi might still be on. Kristi, are you available to comment on this? We haven't formally done this. I think I'm hearing Veena asking that we do this going forward. And so we're taking note of that. And not sure if Kristi still on.

SENIOR STAFF COUNSEL MORIOKA: I am.

MS. HOOVER: Fantastic.

SENIOR STAFF COUNSEL MORIOKA: I am still On. Why don't we -- why don't we take this back as something to look at. And I understand what your comment is, Dr. Singla. So I'm -- we'll give you a response and an answer, and we'll funnel that through Sara.

MS. HOOVER: Yeah. And we can address it publicly at the next meeting as well.

PANEL MEMBER SINGLA: Thank you so much. That's great.

CHAIRPERSON SCHWARZMAN: Thank you for that. Yeah, and I would also -- well, it will be dealt with publicly, but I very much support that request.

Jenny, had a contribution.

PANEL MEMBER QUINTANA: I was just going to further suggest that we follow a model for disclosure like

the American Public Health Association does at their meeting -- annual meetings, where you have a slide included in the slide deck that has to formally --

(Voice in background.)

CHAIRPERSON SCHWARZMAN: There was a little bit of interference there. But as I understand, Jenny was recommending a particular model for that disclosure, if the Program decides to go that way, which is helpful.

Other -- oh, José, please.

PANEL MEMBER SUÁREZ: Just a brief follow-up for that. And that usually comes at the beginning of the presentation, so people know from the beginning, if there are any conflicts of interest.

PANEL MEMBER McKONE: Agreed.

CHAIRPERSON SCHWARZMAN: Okay. So I want to check in one last time with Elizabeth, since according to the agenda, we're still in the time period for open public comment, just make sure that others haven't indicated interest in speaking.

DR. MARDER: Not yet. And we're still checking the email. Last check of the Biomonitoring California email had none from that venue either. So it looks like we do not have public comments at this time.

MS. HOOVER: And this is Sara, just confirming, yes, still no emails coming to the Biomonitoring

California email. So, yeah, I think you can go ahead and wrap-up, Meg.

CHAIRPERSON SCHWARZMAN: Great. Thank you. So thank you all for the contributions to this meeting. Panelists are the visible ones, but the Program staff does a tremendous amount to set up the meeting, and invite the speakers, and organize a really meaningful agenda for us. And the added difficulty of doing that all remotely is not lost on me. So I want to recognize the Program staff and also everybody who joined us to present today, the public commenters, everybody who asked questions. It all enriches the conversation and we appreciate your contributions.

A transcript of this meeting will be posted on the Biomonitoring California website when it's available. And I think as Sara mentioned, the next SGP meeting will be July 16th, 2021 and will be held like this one via webinar.

I want to thank everybody who contributed today and adjourn the meeting.

Thank you.

(Thereupon the California Environmental Contaminant Biomonitoring Program, Scientific Guidance Panel meeting adjourned at 4:19 p.m.)

CERTIFICATE OF REPORTER

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 18th day of March, 2021.

JAMES F. PETERS, CSR
Certified Shorthand Reporter
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