March 2021 Meeting of the Scientific Guidance Panel for Biomonitoring California

Summary of Panel Input and Recommendations

The Scientific Guidance Panel (SGP) for the California Environmental Contaminant Biomonitoring Program (also known as Biomonitoring California) met virtually on March 8, 2021. This document briefly summarizes the Panel's input and recommendations, as well as the range of topics discussed with the guest speakers and audience. Visit the March 2021 SGP meeting page to access the presentations, complete transcript, written public comments, and other meeting materials.

Program Update and Options for Statewide Surveillance

Presentation: Nerissa Wu, Chief, Exposure Assessment Section, Environmental Health Investigations Branch, California Department of Public Health

Panel members discussed the following topics with Program staff:

- Benefits and disadvantages of obtaining samples from the Genetic Disease Screening Program (GDSP) for biomonitoring surveillance, including:
    - More resource efficient approach.
        - Can scale purchase of samples up and down depending on Program budget.
    - Possibility of linking to health-related data and other vital statistics.
    - Inability to return results to individuals, which is a key Program mandate. However, this also confers some benefits in conserving resources and allowing non-targeted screening to be conducted on the samples.
    - Limitations on which analytes can be measured due to sample collection methods and sample volume.
        - Importance of prioritizing which analytes to measure when sample volume is small.
- Benefits and disadvantages of collaborating with Kaiser Permanente on surveillance:
    - Not necessarily representative of the California population, particularly in less populated areas, although this could be addressed through weighting.
    - Good option for surveillance in a limited geographic area.
    - Readily available source of participants, including specific sub-populations of concern (e.g., pregnant women).
    - Costs associated with this option will need to be evaluated.
- Benefits of focused surveillance in one geographic area (using Kaiser or another approach) or in a specific group (e.g., young adults), instead of a statewide study.
    - Possible to get a more representative snapshot in focused surveillance.
    - Build it as a modular study, adding on to it as resources become available.

- Importance of conducting surveillance that allows comparisons over time.
    - Critical for evaluating the impact of chemical substitutions (e.g., replacement phthalates or phthalate alternatives).
- Recommendation to continue to explore the use of existing samples.
    - Looking for ways to link up with COVID-19 and other surveillance programs to obtain samples.
    - Continuing collaborations with outside researchers.
- Probability versus quota sampling for surveillance.
- Possibility of collecting samples (e.g., dried blood spots) by mail and associated concerns (e.g., increased potential for contamination).
    - Suggestion to conduct a small trial of this option.
- Possibility of partnering with NHANES[1] to leverage their work in California.
- Utility of considering other types of biological samples (e.g., hair, nails) that are easier to collect.
    - Issues with potential contamination and representativeness of results from these types of samples were noted, which led to the Program's earlier decision to collect only blood and urine.
    - Possible innovations in collection of alternative types of biological samples will be tracked.
- Recommendation to develop a comparison of the pros and cons of the various surveillance options, including budget comparisons, as a basis for selecting one approach or building a hybrid approach.

Public comment: Nancy Buermeyer of Breast Cancer Prevention Partners outlined her efforts to obtain funding for the Program.

Introduction: Quaternary Ammonium Compounds (QACs) as Potential Priority Chemicals

Introductory Presentation: Shoba Iyer, PhD, Staff Toxicologist, Safer Alternatives Assessment and Biomonitoring Section, Reproductive and Cancer Hazard Assessment Branch, Office of Environmental Health Hazard Assessment (OEHHA)

Document: Potential Priority Chemicals: Quaternary Ammonium Compounds

In the question period after the talk, Panel members:

- Asked if the main sources of QACs are now well known, or if additional sources continue to emerge.
    - Program staff indicated that this information is continuing to be collected, pointing to the recent effort by the Government of Canada (see

[1] National Health and Nutrition Examination Survey conducted by the Centers for Disease Control and Prevention.

https://open.canada.ca/data/en/dataset/b82332e6-3ed3-41f0-af1c-4d173d6e903e).

- Asked how the Program will restrict biomonitoring to industrially produced QACs and not capture endogenous QACs (e.g., choline and carnitine).
    - Program staff noted that listing the entire class would just mean that any QAC could be biomonitored; there would be no obligation to measure naturally occurring compounds.
- Commented that listing entire classes gives the Program the flexibility to select the most relevant chemicals to monitor, potentially as industrial uses shift or as new applications are encountered.

QACs: Detection in the Environment and Degradation Processes

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

The Panel, guest speaker, and audience discussed the following topics:

- Environmental fate and transport.
    - Given the permanent positive charge of QACs, pH effects in environmental media are likely to be minor, but could impact what the compounds sorb to.
    - Carbon chain length likely to be the driving factor for environmental transport, with shorter chain QACs transported farther than longer chain compounds.
    - QACs generally have low volatility and are stable under sunlight radiation.
    - QACs in water will likely stay in water or deposit to sediment.
        - Permanent positive charge essentially prevents water to air transport of free QACs.
    - QACs in air are likely adsorbed to airborne particles (e.g., dust) and not present as free chemicals.
    - Half-lives likely vary from days to weeks in the water column, depending on the specific environmental conditions.
        - Deposition to suspended particles can rapidly remove QACs from lake water to sediment.
    - QACs can contribute to nitrosamine formation in chloramine-treated drinking water and wastewater.
- Screening methods for QACs in Arnold's lab.
    - About half (~12 of 25) of the suspect compounds were identified in the screening analyses, and then added to the list of target QAC analytes.
    - Disinfectant products will be extracted and analyzed to figure out where the peaks will be for QACs that do not have commercially available standards.

- Wastewater treatment plants as a way to study QAC use.
    - Wastewater influent may provide useful samples for quantifying potentially increased use (e.g., during the pandemic).
    - Evaluating municipal versus industrial inputs to wastewater treatment plants is a way to examine sources (e.g., municipal inputs as sources of QACs used in surface disinfection).
- Evidence of increasing QAC use.
    - Production and sales of disinfectants in general increased during the pandemic.
    - Sediment core samples can be collected to examine trends in QAC use. Due to various factors like rate of deposition and sediment movement, a potential peak in lake sediment from increases in use due to the pandemic would likely be observable in 10 years.

Increased Human Exposure to QACs during the COVID-19 Pandemic

Presentation: Amina Salamova, PhD, O'Neill School of Public and Environmental Affairs, Indiana University

The Panel discussed the following topics with the guest speaker:

- Potential for high QAC exposures to specific subgroups, such as custodians and hospital staff.
- Data gaps in exposure information, such as:
    - Exposure potential for individuals spending time in areas frequently disinfected with QAC-containing products (e.g., airplanes, commercial spaces).
    - Exposure potential for other subgroups, defined by age, gender, race, and/or ethnicity.
    - Whether QACs can accumulate and persist in dust over time.
    - Whether QACs are used in disinfectant foggers, and how fogger dispersion could impact potential exposure compared to spraying.
- Probable routes of human exposure based on QAC physicochemical properties and environmental fate.
    - Salamova's team found that benzylalkyldimethyl ammonium compounds (BACs) are enriched in the particle phase, and alkyltrimethyl ammonium compounds (ATMACs) are enriched in the vapor phase.
    - Modeling work published by Li et al. (2020) found that QAC exposure from disinfected surfaces could be high, especially for young children.
    - Indoor air detections of some QACs suggest that the inhalation route of exposure could be important for those compounds. More research is needed on the volatility of QACs.

Analytical Methods for Measuring QACs in Biomonitoring Studies

Presentation: Libin Xu, PhD, Department of Medicinal Chemistry, School of Pharmacy, University of Washington

The Panel, guest speakers, and audience discussed:

- QAC metabolism and absorption.
    - Metabolites produced *in vitro* (e.g., glucuronide conjugates) and those observed so far in urine (e.g., carboxylic acid metabolites were detected, but not hydroxylated metabolites) were discussed.
    - Polymorphism among key metabolic enzymes could impact an individual's QAC metabolic and excretion rates.
    - The need to further examine the protein-binding potential of QACs, and how that relates to bioavailability and half-life in the body, was noted.
    - Organic cation transporters are expressed in the kidneys. QACs can be actively transported into the kidney, where these compounds can accumulate, based on animal data.
- Benefits of different sample matrices for QAC biomonitoring.
    - Urine is the appropriate matrix for identifying polar metabolites, and has the added advantage of convenient sample collection.
    - Blood is useful for examining parent compounds and less polar metabolites.
    - Feces are likely to capture QACs more comprehensively, based on what is known from animal data.
        - Xu's team is measuring parent QACs and metabolites in paired urine and fecal samples for a Biomonitoring California lab pilot study.
- The presence of background levels of QACs, which poses challenges for lab analyses and could indicate a high prevalence of these compounds in the environment.
- The potential for high QAC exposures for individuals spending time in frequently disinfected indoor environments, such as hospitals and schools.

Evaluating the Safety of Quaternary Ammonium Compounds (QACs)

Presentation: Keith Hostetler, PhD, Trinity Consultants and John DeSesso, PhD, Exponent, Inc.

The Panel and guest speakers discussed the following topics:

- Evidence from two earlier presentations at this meeting that some QACs can be absorbed and metabolized, and then detected in human biological samples.
- The potential for volatilization and inhalation of QACs used as disinfectants and the impact of aerosol particle size on respirability.
    - Some QACs have been detected in indoor and outdoor air samples at concentrations higher than other chemicals of concern (e.g., some flame retardants, PCBs, and some pesticides).

- Evaluating chemicals for safety in regulatory animal studies versus human exposure studies.
- Animal studies suggesting that antimicrobial QACs can alter the microbiome.
- The FDA's call in 2016 for additional safety data on antiseptic products, and that additional studies have been conducted or are underway.
- The diversity and broad nature of this chemical class, and that toxicity information for many QACs is not available.

Quaternary Ammonium Compounds as Potential Priority Chemicals: Panel Recommendation

Overview of Potential Priority Chemicals Document on QACs: Shoba Iyer, PhD, OEHHA

Public comment:
ADBAC Issues Steering Committee Comments on Analytical Methodology for QACs
Women's Voices for the Earth Comments on QAC Exposures to Vulnerable Populations
Women's Voices for the Earth Comments on FDA Evaluation of ADBAC Data Gaps

Additional public comment (received after March 8, 2021):
Hostetler KA, Fisher LC, Burruss BL (2021). Prenatal developmental toxicity of alkyl dimethyl benzyl ammonium chloride and didecyl dimethyl ammonium chloride in CD rats and New Zealand White rabbits. Birth Defects Res, 21 March 2021, doi: 10.1002/bdr2.1889. Epub ahead of print.

Teratology Working Group (2021). Status Report on the Systematic Review of Quaternary Ammonium Disinfectant Compounds for Developmental and Reproductive Toxicity.

In deliberating on QACs as potential priority chemicals, Panel members highlighted:

- Significant data gaps in exposure information.
- The high potential for exposure to the public and specific subgroups in California, such as custodians and hospital staff.
- The potential for increased exposures during the COVID-19 pandemic given frequent disinfection practices.
- The importance of adding QACs to the list of priority chemicals as chemical production is rising, to detect potentially increasing trends in exposures.
- Known human health effects, such as asthma, and emerging toxicity concerns observed in laboratory studies.
- Recent studies showing the ability to biomonitor some QACs in urine and blood collected from the general population.

Veena Singla motioned that the class of quaternary ammonium compounds be included as priority chemicals for the [California Environmental Contaminant] Biomonitoring Program and Carl Cranor seconded the motion. The Panel voted unanimously in favor of this motion. José

Suarez did not vote because he had to miss some of the presentations on QACs. Veena Singla was inadvertently not polled, so her vote was not recorded.

Open Public Comment Period

Nancy Buermeyer from Breast Cancer Prevention Partners commented on the importance of Biomonitoring California's list of priority chemicals, which is one authoritative source of Candidate Chemicals for the Safer Consumer Products program (implemented by the Department of Toxic Substances Control). Lists like these have been valuable in crafting legislation to require chemical ingredient disclosures and raising awareness about chemicals in consumer products.

Veena Singla suggested that future SGP meeting presenters explicitly disclose funding sources and any conflict of interest, which can be important for the Panel to evaluate the research being shared. Several other Panel members supported this suggestion.