**July 2020 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 on July 14, 2020, via webinar. This document briefly summarizes the Panel's input and recommendations, as well as the range of topics covered in the afternoon discussion session with the guest speakers and audience. Visit the July 2020 SGP meeting page to access the presentations, transcript, and other meeting materials.

## Program and Laboratory Updates

Presentation: Nerissa Wu, Chief, Exposure Assessment Section (EAS), Environmental Health Investigations Branch (EHIB), California Department of Public Health (CDPH)

Presentation: Jianwen She, PhD, Chief, Environmental Chemistry and Biomonitoring Branch, Environmental Health Laboratory (EHL), California Department of Public Health (CDPH)

Presentation: June-Soo Park, PhD, Chief, Environmental Chemistry Laboratory (ECL), California Department of Toxic Substances Control (DTSC)

Panel members discussed the following topics:

- Possible alternatives for sample collection in the California Regional Exposure (CARE) Study given the COVID-19 emergency
    - Urine kits with clear instructions for at-home collection are an option; however, this approach would preclude measurement of perfluoroalkyl and polyfluoroalkyl substances (PFASs), which are of significant concern in California.
- AB 617 biomonitoring planned approach
    - Key elements include:
        - Biomarkers of exposure, such as metabolites of polycyclic aromatic hydrocarbons (PAHs) and volatile organic compounds (VOCs)
        - Biomarkers of effect
        - Complementary measurements (e.g., air monitoring; particle speciation; non-targeted screening)
    - Importance of measuring cotinine and potential markers of vaping and tobacco and marijuana smoke to support biomonitoring data interpretation was noted.
    - If genotoxic measures of effect are considered, folate levels should be measured.
- Technical challenges with non-targeted analysis (NTA)
    - Collaborating with external partners and using all available tools when processing data from NTA was emphasized as important.
    - Further mining the data to assess potentially varying NTA results across the population, particularly any differences in disadvantaged communities, was discussed.

- Consumer products exposure database developed by the California Air Resources Board (CARB) as a potential source of chemicals to prioritize for methods development
- Characteristics of chemicals that tend to be higher in maternal serum versus cord blood
    - Data analyses to examine this are still in progress.
- Halogenated carbazoles
    - Application of structure-activity analyses was proposed as a way to estimate exposure potential of class members and better target biomonitoring studies.
    - This class is not a "designated chemical" under Biomonitoring California (post-meeting follow up verified that it is not captured in the currently listed group of "brominated and chlorinated organic compounds used as flame retardants").

Public comment: Dr. Jay Murray commented that molybdenum is an essential element, and the geometric mean values reported in urine samples (from the California Regional Exposure Study) are consistent with what is known about dietary intake.

**Non-Targeted Analysis Presentations**

**Findings from US EPA's Non-Targeted Analysis Collaborative Trial (ENTACT)**
Presentation: Jon Sobus, PhD, Center for Computational Toxicology and Exposure, US Environmental Protection Agency (US EPA)

**Multimedia Exploration of Emerging PFASs and Their Sources**
Presentation: James McCord, PhD, Center for Environmental Measurement and Modeling, US EPA

**Data Science and Cheminformatics Tools to Support Exposomics and Metabolomics**
Presentation: Dinesh Barupal, PhD, Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai

**A Multi-Platform Non-Targeted Framework for Measuring the Human Exposome**
Presentation: Doug Walker, PhD, Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai

**Chemical Suspect Screening as a New Approach to Biomonitoring: An Application in Firefighters and Office Workers**
Presentation: Rachel Morello-Frosch, PhD, MPH, Department of Environmental Science, Policy and Management & School of Public Health, University of California, Berkeley

Topics covered in the question periods after the presentations included:

- Performance metrics for NTA approaches, such as resolution versus precision
    - ENTACT will help address this; analyses of results still underway.
- Evaluation of chemical properties to inform NTA – i.e., predicting chemicals likely to be prevalent and have higher exposures.
    - This could include molecular modeling, exposure modeling, and pharmacokinetic modeling.

    - Modeling can also help identify appropriate methods for observing certain types of chemicals.
- Chemicals that can be missed in these NTA approaches, such as quaternary ammonium compounds that have a permanent positive charge
- Communicating to study participants and the community about NTA findings on PFASs about which little is known
- Development of a "guidebook" for application of comprehensive multimedia approaches to understanding emerging chemicals, such as what was done for PFASs
- The complexities of conducting NTA on less-known emerging chemicals, versus a well-recognized class like PFASs
- Approaches for mining large data repositories like GNPS[1] to map non-targeted spectra to compounds
- Sensitivity of NTA in identifying environmental chemicals, given the often very low concentrations in biospecimens, and strategies to address this (e.g., increasing sample volume)
- Applying multi-platform NTA frameworks in well-characterized, targeted populations, with the ultimate goal of generalizing the approach to broad surveillance
- Incremental improvements in the extent of chemical compounds detected via NTA
    - There is a long way to go before the totality of the chemical space is captured.
- The importance of making spectral libraries public
- Educating study participants about NTA and engaging them in the study design
- Prioritizing which targeted analyses to carry out based on NTA results, taking into account goals of the study and resources
- Results from NTA and targeted analyses that would be useful to participants in the women firefighters study
    - Identifying potential associations between measured chemical exposures and breast cancer was a priority for study participants.
    - An important outcome of that study was to identify chemicals for immediate action in terms of reducing exposures and improving work practices.

**Afternoon Discussion Session**

Questions that were posed to inform the afternoon discussion included:

- What are some possible next steps for Biomonitoring California in the area of NTA?
    - Should the Program consider conducting additional pilot NTA projects?
    - What challenges do you envision as we move forward in applying NTA to Biomonitoring California's work?
- Are there opportunities to leverage ongoing NTA work by other groups, or collaborate with those researchers to support Program goals?
- Are there emerging chemicals or chemical groups being identified through NTA that should be reviewed by the Program as potential designated chemicals?
- What suggestions do you have on approaches for returning NTA results to study participants?

[1] Global Natural Products Social (GNPS) Molecular Networking, an interactive online chemistry-focused mass spectrometry data curation and analysis infrastructure

The Panel, guest speakers, and audience discussed the above questions and other topics, including:

- PFAS findings from site investigations
  - Proliferation of new PFASs, which are replacing the legacy PFASs that had a more narrow chemistry, is resulting in site-specific contamination dependent on the major producer or user at that location.
  - Different sites tend to have different major contaminants (e.g., GenX).
  - Removing the source quickly reduces PFAS concentrations; environmental breakdown appears not to be a significant removal pathway for most of the compounds studied.
- Coverage of PFASs in NTA methods
  - Volatile PFASs tend not to be captured.
  - Total organic fluorine-type methods are being applied as one way to achieve better coverage.
- The importance of examining real-world samples, in addition to standardized mixtures to evaluate the performance of NTA methods
- The need to standardize reporting of confidence levels for NTA findings
  - Third-party credentialing of environmental NTA is one possible outcome of ENTACT.
  - Conveying confidence levels and uncertainties is complex and challenging to do in an accessible and transparent way for target audiences, including researchers and study participants.
  - Ideally, NTA findings should be confirmed by pure standards to report results with confidence, particularly to study participants.
- Applying NTA proactively for early identification of chemicals of concern, including regrettable substitutions, manufacturing byproducts that are not covered by current regulations, and emerging chemicals for which almost nothing is known
  - Bringing NTA results and rapid toxicity screening into regulatory submission packages for pre-market approval would be an important step.
  - Focus on looking forward not back: Use a portfolio of tools that includes NTA to find out what is in the population now and what might be appearing in the future due to shifts in the market.
- Potential application of silicone badges in Biomonitoring California studies
  - Limitations include lack of quantification of measured levels, making these more useful as a screening tool.
- Advantages of using untargeted metabolomic platforms that can characterize biological processes and link them to exposure biomarkers
  - Development of “exposome risk scores” could also act as biomarkers of disease once a better understanding is developed of how exposure profiles contribute overall to health outcomes.
- Recommendation that the Program design an NTA pilot project in a specific population, such as a disadvantaged community, a specific occupational group, a refugee group, or another group relevant to California’s unique population.
  - NTA strategies could be focused on chemical classes of concern in the particular group or community (i.e., applying a semi-targeted approach instead of NTA).

    - Collaborating with the potential participants in designing the NTA study and clearly conveying the benefits and potential pitfalls is important.
    - Biomonitoring California's major priorities should be considered when designing NTA projects.
    - Addressing study participant needs, including development of high quality results return materials, is essential.
- Importance of examining cumulative burden of exposures (including chemical and non-chemical stressors) in heavily impacted communities and looking for ways to apply NTA to that type of assessment
- Using NTA results to inform policy decisions, such as facility siting, in heavily impacted communities
- Practical and feasible ways to apply NTA
    - Using environmental samples instead of biospecimens is one approach to consider.
    - Look for opportunities to apply NTA to samples that have already been characterized using targeted methods.
    - Consider NTA projects on biobank samples that would not require results return to participants.