National Toxicology Program

Board of Scientific Counselors

April 23, 2021

National Institute of Environmental Health Sciences
Research Triangle Park, NC

Summary Minutes

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1. Abbreviations and Acronyms

ALI	Air-liquid interface
BSC	Board of Scientific Counselors
COVID-19	Coronavirus Disease 2019
DNTP	Division of the National Toxicology Program
ECIC	Emerging Contaminants and Issues of Concern
EWG	Environmental Working Group
MPS	Microphysiological systems
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NHANES	National Health and Nutrition Examination Survey
NTP	National Toxicology Program
OIE	Occupational and Inhalation Exposures

2. Attendees[1]

Board of Scientific Counselors

Chair: David Eaton, PhD, University of Washington
David Berube, PhD, North Carolina State University
Eric Blomme, DVM, PhD, AbbVie (*ad hoc*)
Weihsueh Chiu, PhD, Texas A&M University
Susan Felter, PhD, Proctor & Gamble
Kathleen Gray, PhD, University of North Carolina, Chapel Hill (*ad hoc*)
Matthew Martin, PhD, Pfizer, Inc. (*ad hoc*)
Devon Payne-Sturges, DrPH, University of Maryland, College Park (*ad hoc*)
Mark Russi, MD, Yale University (*ad hoc*)
Anne Ryan, DVM, PhD, Act 5 Ventures, LLC
Veena Singla, PhD, Natural Resources Defense Council (*ad hoc*)
Susan Tilton, PhD, Oregon State University

National Institute of Environmental Health Sciences/National Toxicology Program (NIEHS/NTP) Staff

Rick Woychik, PhD

National Institute of Environmental Health Sciences/Division of the National Toxicology Program (NIEHS/DNTP) Staff

Brian Berridge
Chad Blystone
Mark Cesta
Suzanne Fenton
William Gwinn
Michelle Hooth
Daven Jackson-Humbles
Gloria Jahnke
Angela King-Herbert
Ruth Lunn
Elizabeth Maull
Esra Mutlu
Kristen Ryan
Sheena Scruggs
Stephanie Smith-Roe
Matthew Stout
Mary Wolfe
Pei-Li Yao

Other Federal Agency Staff

Gonçalo Gamboa da Costa, U.S. Food and Drug Administration (BSC liaison)
Elizabeth Whelan, National Institute for Occupational Safety and Health (BSC liaison)

Contract Support Staff

Canden Byrd, ICF
Sarah Colley, ICF
Ernie Hood, Bridport Services
Jeanne Luh, ICF
June Mader, GOFORWARD LLC
Blake Riley, ICF
Samantha Snow, ICF

Public Attendees

Alexis Temkin, Environmental Working Group

[1]The meeting was webcast with the listed individuals attending by Zoom. NIEHS/DNTP staff are limited to those with a role in the meeting. Public attendees are limited to those presenting oral comments.

3. Introductions and Welcome

The National Toxicology Program (NTP) Board of Scientific Counselors (BSC) convened on April 23, 2021 via Zoom for identified attendees noted above and webcast for public attendees. Dr. David Eaton served as chair. Dr. Sheena Scruggs served as the Designated Federal Official.

Dr. Eaton called the meeting to order at 12:30 p.m., welcomed everyone to the meeting, and asked BSC members, Drs. Rick Woychik, Brian Berridge, Sheena Scruggs, Gonçalo Gamboa da Costa, and Elizabeth Whelan to introduce themselves. He noted that board members Drs. David Michaels and Pamela Lein would not be in attendance. Dr. Scruggs read the conflict-of-interest policy statement and briefed the attendees on meeting logistics.

4. Introduction to the Meeting Agenda

Dr. Berridge, Associate Director of NTP and Scientific Director of the Division of the NTP (DNTP), introduced the meeting's agenda.

He reviewed the four strategic areas of focus in the DNTP portfolio and discussed the agenda of upcoming 2021 BSC meetings.

He reflected upon the feedback from the February 2, 2021 BSC meeting, in which board members were asked the following three questions in a survey:

- Was BSC engagement at the right strategic level to enable valuable input to DNTP's direction and work?
- What went well, specifically?
- What can we do better next time?

Survey responses showed that all respondents felt that the engagement met or exceeded expectations. Respondents suggested that there should be a broader discussion of the discussion questions, with more time devoted to the discussions and fewer, simpler questions.

Dr. Berridge described the elements of continuous improvement for BSC meetings based on the feedback received.

- Fewer, simpler discussion questions
- No lead discussants
- Whole group facilitation process involving the BSC and Program Management Teams, rather than breakout group sessions
- The chair and Dr. June Mader will facilitate discussion with the aim of broader engagement.

Dr. Berridge expressed a fond farewell to Dr. Whelan since this will be her final BSC meeting before she retires. He also issued a special thank you to Dr. John Bucher, NTP senior scientist and former Associate Director of NTP, who is retiring after more than 30 years at the National Institute of Environmental Health Sciences (NIEHS) and NTP. Dr. Woychik, NIEHS and NTP Director, added his gratitude to Dr. Bucher for his service. Dr. Eaton also thanked Drs. Whelan and Bucher.

Dr. Eaton noted that there were no clarifying questions from the BSC members.

5. Occupational and Inhalation Exposures Program

Dr. Kristen Ryan briefed the board on the Occupational and Inhalation Exposures (OIE) program. Dr. Kristen Ryan began by adding her thanks to Drs. Whelan and Bucher and then introduced the OIE Program Management Team, which consisted of Drs. Mark Cesta, William Gwinn, Michelle Hooth, Daven Jackson-Humbles, Angela King-Herbert, Kristen Ryan, Matthew Stout, and Pei-Li Yao. She presented background information about the adverse health outcomes associated with OIEs, indicating that chronic respiratory diseases were the third-leading cause of deaths worldwide in 2017. Indoor and outdoor air pollution can affect the development of respiratory diseases. Furthermore, socioeconomic status, climate, genetics, and occupation can enhance adverse health outcomes. Hazard characterization is critical to creating a safe living and working environment and reducing disease burden following inhalation exposures.

Dr. Kristen Ryan described DNTP's experience evaluating complex exposures, including reporting or publishing more than 100 studies. DNTP's technical capabilities are established, unique, and robust. When needed, DNTP also develops partnerships and collaborations to address specific exposures to physical or biological agents. Dr. Kristen Ryan provided examples of several current projects monitored by the OIE program. She listed federal stakeholders in the program.

Dr. Kristen Ryan listed the three OIE program objectives:

- Objective 1: Assess health hazards of airborne substances
- Objective 2: Expand capabilities for predicting adverse health effects
- Objective 3: Enhance the translational relevance of experimental models

To illustrate how the objectives are being achieved, she provided details about studies of: α-pinene, a common flavoring and fragrance ingredient and a major component in turpentine; novel and alternative technologies that have emerged to investigate inhalation toxicology in human airways including *in vitro* models and microphysiological systems; and the incorporation of physiological monitoring in recent rodent inhalation studies. For each objective, she discussed short-term (1–2 years), medium-term (2–4 years), and long-term (4–5 years) strategies.

In summary, DNTP has established, robust, and unique capabilities to conduct assessments for inhalation and workplace exposures, with expertise from partnerships and contract capabilities. The OIE program was formed to manage current projects and emerging public health problems related to inhalation exposures and to utilize resources and infrastructure to systematically and robustly build capabilities (i.e., novel tools and approaches).

Dr. Kristen Ryan concluded the presentation by asking the OIE team members (listed above) to introduce themselves.

Clarifying Questions

Dr. Anne Ryan asked whether skin exposures will be part of the OIE program since they were mentioned in the Problem Statement but not in the briefing document. Dr. Kristen Ryan replied that dermal exposures and other occupational exposures (e.g., ocular exposure) are included in

the program, although the program focuses on inhalation exposures since this exposure route is a major cause of occupational disease and mortality.

Dr. Eric Blomme asked about the role of immune toxicity endpoints in the evaluation of inhalation toxicology. Dr. Gwinn replied that immunotoxicology studies have been conducted in the past and will be conducted in the future, within the subchronic and chronic inhalation studies. Dr. Gwinn added that there are ways to incorporate the flow of circulating immune cells into the model *in vitro* systems, such as lung-on-a-chip. He agreed that immune responses can impact toxicity to inhaled compounds.

5.1. Written Public Comments

Dr. Eaton noted that the board received two written public comments, one from Pamela Garcia, a private citizen, and one from Dr. Alexis Temkin, a toxicologist with the Environmental Working Group (EWG).

5.2. Oral Public Comments

Dr. Temkin also presented oral public comments regarding the OIE program. In general, EWG supports and recognizes the need for and strength of the OIE program. DNTP should, however, broaden the scope of the program to highlight exposures associated with cleaning products used by the public, as well as professional and domestic cleaning workers, janitors, and people who clean as part of their job duties. Children's health should also be more prominent throughout the program. More research is needed to understand these complex mixtures and molecular mechanisms that link cleaning products and occupational exposures to adverse respiratory outcomes, and DNTP is in a unique position to address those issues. Dr. Temkin remarked that characterizing the health risks associated with cleaning products is particularly important given the impact of the COVID-19 pandemic on consumer cleaning behavior and the concomitant increase in sales of cleaning products.

Dr. Kristen Ryan thanked Dr. Temkin for her remarks and noted that DNTP has conducted studies in conjunction with the National Institute for Occupational Safety and Health (NIOSH) in this area.

5.3. BSC Discussion

Board members were asked to consider three questions.

5.3.1. First Question

Consider the Problem Statement, Objectives, and Value Proposition in the Program Concept document:

Share your insights regarding whether there is clean alignment among the three. For example, do the Objectives align with the Problem Statement? Does the Value Proposition match what is being stated in the Problem Statement?

Dr. Eaton commented that the OIE program's example of α-pinene represented an area of great interest—natural products. He discussed a previous NTP study on *d*-limonene, another natural substance, which showed the importance of understanding mode of action since adverse effects from exposure appear to be species specific.

Dr. Susan Felter suggested that the Problem Statement should include some reference to what would be considered normal exposures to chemicals, such as α-pinene, that occur naturally and are found in our diet. The focus on translational relevance may be a new approach that NTP has not necessarily considered in the past. She mentioned studies that have shown potential health benefits from α-pinene and other monoterpenes. Including such considerations would present a fuller understanding of human responses to exposures to that particular chemical.

Dr. Eaton felt there was good alignment between the Problem Statement, Objective, and Value Propositions. There are, however, challenging scenarios to be considered, such as radiofrequency radiation exposures. It is important to understand the mode of action and basic toxicology of substances for extrapolation from animal models to humans. He reiterated the value of doing mechanistic studies to understand human relevance.

Responding to Dr. Felter's comment, Dr. Kristen Ryan noted that DNTP is actively pursuing studies such as those she suggested and the OIE program will continue to use mode of action and toxicokinetic studies to ensure that the exposures conducted in rodents are relevant to humans.

Dr. Susan Tilton asked whether there are plans to address individual variability or susceptibility with *in vitro* models, particularly given that cells could be cultured from different donors. Dr. Gwinn said that in the air-liquid interface (ALI) models, donor cells from different human individuals can be acquired. Some of the commercial vendors have cells from multiple donors, both healthy and those with underlying respiratory diseases and other comorbidities or susceptibility factors.

Dr. Devon Payne-Sturges addressed the issues of human variability and mechanism of action. She mentioned increasing concern and evidence that the combination of chemical exposures with nonchemical exposures, such as psychosocial stress, creates synergistic effects. Psychosocial stress occurs in the workplace and in the community. She asked to what extent the OIE program is considering developing models that would bring those constructs together in animal models to improve their relevance. Dr. King-Herbert responded that the OIE program recognizes that keeping rodents in cages can be stressful. A program has been implemented to give study animals environmental enrichment to alleviate some of the stressors, including conditions that allow species-specific behaviors. In inhalation studies, the animals are acclimated to the systems before exposures are started. For whole-body exposure studies, the OIE program is examining the feasibility of housing animals in polycarbonate cages and only moving animals into inhalation chambers during exposure periods. Dr. Payne-Sturges then clarified that she was asking about developing animal models that are relevant to the stress that humans experience, which include both nonchemical and chemical exposures. Dr. Kristen Ryan explained that Dr. King-Herbert is working on helping to define the levels of stress experienced by the animals. By establishing a baseline of stress, it would allow for analysis of other types of stressors. Dr. Stout added that they are exploring studies using physiological monitoring to establish a baseline stress level and how certain conditions and procedures might change the baseline.

Dr. Matthew Martin expressed confusion about the real connections in the *in vitro* to *in vivo* continuum, other than on the back end with the translation work. He asked whether there are plans in some of the pilot studies of microphysiological systems (MPS) to test compounds on the program's "bucket list." He wondered how much DNTP is taking the lead, versus some of the private consortia and other groups working on MPS systems. He asked whether the group had

given thought to the growing area of more real-world data. Dr. Gwinn explained that the goal with the *in vitro* models is to start by testing compounds that have previously been tested *in vivo* in rodents with known lung effects. Those chemicals will be run through both the ALI and lung-on-chip systems to see how well the *in vitro* data correlate with the effects seen *in vivo*. Proof of concept will provide confidence moving forward whether the *in vitro* models can be used for more predictive studies using unknown or lesser-known chemicals. He described collaborations with the National Center for Toxicological Research and Battelle for exposure studies with ALI and lung-on-chip systems. Dr. Stout elaborated on the Battelle partnership.

Dr. Weihsueh Chiu had three short comments. The first related to the challenges of nonchemical stressors, which are challenging to measure to ensure that experimental animals receive the right dose. He cited two issues regarding inhalation studies involving toxicokinetics and dosimetry. Respiratory tract effects also involve both toxicokinetic and toxicodynamic components. In order to move toward a more translational and more *in vitro*-based mechanistic approach, a key characteristics effort on respiratory toxicants might be useful. Dr. Kristen Ryan appreciated the board's ideas regarding key characteristics and real-world exposures.

5.3.2. Second Question

Consider the Problem Statement, Objectives, and Value Proposition in the Program Concept document:

Share your insights on whether there is sufficient focus to deliver the intended value to stakeholders.

Dr. Kathleen Gray commented that many of the interactions with stakeholders appeared to be federal consortia and working groups, and given the importance of occupational exposures, she asked about interactions with partners who could provide direct contact with workers, a sense of worker exposures, and which exposures were the most pressing. Dr. Kristen Ryan agreed that there has historically been extensive contact with federal partners who have direct contact with many stakeholders, worker industries, advocacy groups, and industry partners; however, the OIE program does not typically work directly with these groups. Although there could be more interaction with the public and advocacy groups in the future, the OIE program currently relies on the strong relationships and formal processes their partners have already established. Dr. Whelan noted that NIOSH has a process for deciding what is important to study from a worker perspective and then working with NTP partners on agents of mutual interest. NIOSH goes into the workplace and studies workers directly, although that is often challenging. She emphasized the importance of the dermal exposure route and of psychosocial stress, and that these were not easy topics to address.

Dr. Eaton felt that the focus in the program is good, although he remains concerned about basic challenges in dose-response analysis with the kinds of exposures being considered and he reiterated how useful mode of action can be in characterizing hazard of specific substances. He agreed with previous comments about the interaction of stress with exposure to a toxic substance, citing a colleague who conducted studies with an MPS looking at a nephrotoxic substance and found that heat stress on cells caused a tremendous interaction. He noted that investigating how stress response modifies toxic response fits well within the OIE program.

Dr. Payne-Sturges noted that in the Program Concept document, the OIE program expressed a desire to expand the array of stakeholders, and she wondered how that would be done. Dr. Kristen Ryan said that since their work has been driven by agency partners, expanding stakeholders is a new area for the group to focus on. She provided examples from other areas of DNTP, such as the Health Effects Innovation program, that the OIE program could model to reach out to stakeholders.

Dr. David Berube was unsure who the broader array of stakeholders is and expressed that it is an ambitious idea. He wondered how the effort would be assessed. Dr. Stout replied that there is a research program on the effectiveness of DNTP projects. Although it is difficult to assess, DNTP is very interested in doing so. Dr. Kristen Ryan agreed that it is a lofty goal for the group to be effective in so many ways and reach out to so many people, and she agreed with Dr. Berube's observation that such outreach should not be an afterthought. Dr. Kristen Ryan noted that as a new chemical is nominated to assess, DNTP looks for new stakeholders, such as specific advocacy or academic groups. There are efforts to identify groups up front and not at the very end of the process. Dr. Gwinn added that DNTP inhalation studies can be used by the Report on Carcinogens for evaluations, and chronic studies are widely used by other agencies for hazard assessments. Dr. Mary Wolfe thanked the board for its useful comments on outreach and the effectiveness of DNTP's work. She added that it is an area DNTP hopes to strengthen and expand, including work on developing a model for bibliometrics and the broader range of DNTP impact, such as informing regulations, policy changes, and use at the state, local, and international levels. It is extremely important to DNTP to know that its work is having an effect on public health and public health policies. Work will also continue to understand how to effectively communicate DNTP findings to the public.

Dr. Felter commended DNTP for its sincere and rigorous outreach to all stakeholders who may be interested in or affected by the research. Citing the example of α-pinene, she urged the inclusion of research going on elsewhere on low-level exposures, whether dietary or inhalation, and potentially even looking at anticancer activity of α-pinene. That would give the full picture to stakeholders who assess the safety of chemicals. Dr. Kristen Ryan asked Dr. Felter if she had any specific ideas for products to communicate with the public. Dr. Felter felt that multiple ways of doing so are needed. Dr. Felter suggested a layman's versions of NTP Technical Reports and Report on Carcinogens, and she wanted more attention drawn to information on low-level exposures to chemicals that may provide health benefits, such as α-pinene.

Dr. Berube suggested studying how different types of stakeholders respond to information. The risk communication community could help develop protocols to reach different levels or types of stakeholders, who may require distinctly different communication approaches. The goal is to turn people from information receivers to information seekers.

5.3.3. Third Question

Looking ahead, what do you see as the top opportunity or challenge in this Program?

Dr. Mader read the question and introduced the board to the online tool MURAL, which functions as a virtual whiteboard. BSC members were given five minutes to post their individual responses in the MURAL platform, which was visible to meeting attendees in real time.

BSC members' written responses from the MURAL activity are provided below (see Attachment A for actual MURAL output).

- Dr. Berube: This is a remarkable program that will be challenged as the stakeholder population diversifies. Developing protocols for just such an occasion would be a good tool.
- Dr. Blomme: Validation of new proposed *in vitro* models, including understanding of translatability to humans and of performance characteristics.
- Dr. Chiu: Prioritizing among the many potential inhalation toxicants to maximum public health impact.
- Dr. Eaton: Interfacing with NIOSH and industry to obtain 'real world' exposure levels that can help to design human-relevant *in vitro* and *in vivo* studies.
- Dr. Felter: Inhalation models that address complex human exposure scenarios, including short-term, intermittent.
- Dr. Gray: Engaging effectively with non-federal (and non-industry?) stakeholders.
- Dr. Martin: Balancing assessment of high priority occupational or inhalation toxicants while evaluating and advancing next generation approaches like MPS and real-world data.
- Dr. Payne-Sturges: Chemical and non-chemical exposures in the workplace and their synergistic effects; increase in use of cleaning products due to COVID, including inside schools.
- Dr. Mark Russi: Adequacy of animal and *in vitro* models to reflect dysfunctional immune responses.
- Dr. Anne Ryan: Balanced portfolio (concept->communication) with operational efficiency and speed to stakeholders; assess impact of data reported – does it result in changes in exposure?
- Dr. Veena Singla: Ensure data are informing mitigation of health risks.
- Dr. Tilton: Opportunities for non-occupational exposures/stakeholders.

After all responses were received from the board, OIE program team members internally discussed the responses while other attendees were on a break. Dr. Mader then reintroduced the OIE program and invited team members to share their thoughts about the board's responses.

Dr. Stout noted the common theme of prioritization. In terms of inhalation studies, much depends on the feasibility of the testing, so feasibility work is often done before the team even considers a particular study design. He cited studies on naturally occurring asbestos as an example of the process and discussed several other examples.

Dr. Gwinn discussed previous studies of artificial butter flavorings as another example of prioritization. He described how the group has taken data from exposures in humans and extrapolated it across both *in vivo* and *in vitro* models, providing a model for a process to be used with other potential agents of concern.

Dr. Eaton commented that Dr. Gwinn's example was wonderful and that it was exactly what he would like to see more of emerging from the OIE program. It was a real-world problem in which state-of-the-art, new tools were used to elucidate mechanisms.

Dr. Kristen Ryan observed that as new *in vitro* models are developed, it will allow the screening of more chemicals, and classes of chemicals, for toxicity.

Dr. Gwinn noted that DNTP recently released a toxicology report for TMSD (trimethylsilyldiazomethane), a chemical that chemists were exposed to in laboratories and caused two fatalities. DNTP developed an *in vivo* animal model that replicated some of the findings from the fatalities. It was another example of taking exposures in humans and then developing an animal model.

Dr. Yao remarked that the NTP Interagency Center for the Evaluation of Alternative Methods is investigating alternative approaches to animal use for use with emergent issues.

Dr. Kristen Ryan asked board members for more clarification on comments regarding ensuring that data are informing mitigation of health risks. Dr. Singla felt that a strength of the program is its connection and collaboration with federal agencies, with hazard characterization data feeding into the work of the other agencies, informing categorization and exposure limits. She added that her comment had been specific to Objective 2 and the *in vitro* systems. She asked what other criteria or characteristics are needed to ensure that those data can continue to connect with policy decision and the mitigation of health risks. Dr. Kristen Ryan thanked Dr. Singla for the helpful feedback.

6. Emerging Contaminants and Issues of Concern Program

Dr. Esra Mutlu briefed the board on the Emerging Contaminants and Issues of Concern (ECIC) program.

Dr. Mutlu began by congratulating Drs. Whelan and Bucher on their upcoming retirements and then introduced the ECIC program team, which consisted of Drs. Chad Blystone, Suzanne Fenton, Gloria Jahnke, Ruth Lunn, Esra Mutlu, and Stephanie Smith-Roe. The ECIC is one of the DNTP Responsive Research Programs. The program is intended to address:

- Emerging issues and emergencies arise unexpectedly yet regularly that require high-quality, actionable data to protect public health.
- Rapid mobilization of scientific resources in response to such situations can be challenging.
- Responsive programs would need to communicate translationally relevant data in a timely manner for public health decision making.

Dr. Mutlu described the many reasons why a program like ECIC is needed at this point in time, and why NTP is the ideal agency to address those needs. She discussed the ECIC program objectives:

- Objective 1: Address emerging issues where DNTP may apply capabilities and expertise to effectively respond to public health issues in a timely way using a 'Decision Framework'

- Objective 2: Use 'horizon scanning' or scoping activities to proactively identify emerging contaminants and issues of concern, especially pertaining to historically marginalized populations.
- Objective 3: Formulate and apply strategic approaches, leveraging the breadth of DNTP capabilities that allow for fit-for-purpose research responses to emerging contaminants, diseases, disasters, or other concerns

Dr. Mutlu provided more details about the first objective, including *what* (does it meet the ECIC program's definition for emergency, emerging contaminants, or issue of concern?) and *how* (does it require "responsive research" consistent with the ECIC program's problem statement?). She illustrated the flow of the decision framework. Objective 2 involves proactive identification of future issues. Objective 3 involves the identification of strategies for prioritized response, including assessing the problem, choosing the means of addressing it, doing the necessary homework, and networking with other stakeholders. It requires coordination and regular communication to formulate an ECIC Prioritized Project Plan. Dr. Mutlu described several examples of the process at work, including chronic kidney disease of unknown origin, glyphosate, boron, and sulfolane. She acknowledged the involvement of the many program stakeholders and mentioned milestones or current project stages of the ECIC program's projects.

She discussed the program's strategic objective milestones and the status of each of the three objectives in the context of short-term (0–1 year), mid-term (1–2 years), and long-term (2–4 years) developments.

Dr. Mutlu concluded the presentation by asking the ECIC team members (listed above) to introduce themselves.

Clarifying Questions

Dr. Blomme asked the ECIC program to elaborate on their approach to horizon scanning and scoping and if there is a way to make it an efficient and useful process. Dr. Fenton expressed that the overall goal is to obtain relevant and credible evidence on what the ECIC program should prioritize. To do so, the program has identified a number of stakeholders to consult. The group has met with 10, and will meet with 10–12 more, to develop a list of what the stakeholders think is most important. The group is also attending meetings and relevant webinars on emerging concerns and issues.

Dr. Tilton asked how the program handles engagement with and translation of data to affected communities. Dr. Mutlu agreed that it was a very important topic and will depend on communication with stakeholders to determine how to improve in that area. Dr. Lunn reiterated that the team works with Dr. Wolfe's group on communicating to all external audiences. Dr. Blystone said that in the past, the group had worked through stakeholders, who have their own means of communication and translation to their audiences.

Dr. Berube asked whether the ECIC program's approach to horizon scanning is interviewing people selected as experts. Dr. Mutlu replied that the approach is to consult with stakeholders and others about their thoughts on emerging contaminants and issues of concern. Dr. Berube noted that many tools have been developed to aid the process and he agreed to speak further with the ECIC program on the subject. Dr. Fenton added that the group also wants to hear from

environmental justice groups and advocacy groups, especially those based in North Carolina. The effort is intended to go beyond typical stakeholders.

6.1. Written Public Comments

Dr. Eaton noted that no written public comments had been received.

6.2. Oral Public Comments

Dr. Eaton noted there was a request to present oral public comments from Theodora Scarato of Environmental Health Trust, however, Ms. Scarato did not attend the session.

6.3. BSC Discussion

Board members were asked to consider three questions.

6.3.1. First Question

Consider the Problem Statement, Objectives, and Value Proposition in the Program Concept document:

Share your insights regarding whether there is clean alignment among the three. For example, do the Objectives align with the Problem Statement? Does the Value Proposition match what is being stated in the Problem Statement?

Dr. Eaton noted that one of the biggest challenges in terms of alignment is that, by the nature of the program, it is a moving target.

Dr. Singla supported the program's direction to go from reactive to proactive in identifying emerging contaminants and issues of concern. She asked whether there had been any thought to the need for identification of unknown chemicals. Dr. Mutlu responded that it had been a topic of discussion within the program and with other programs. The intention is to go to nontargeted analysis, focusing beyond the "known suspect" list and using other tools for horizon scanning. Dr. Fenton added that one of the projects in the queue is focused on evaluating cord blood from Black and non-Black communities to investigate whether there are environmental health disparities.

Dr. Martin discussed the reactive elements of the program, such as responses to the Gulf Oil spill and the Elk River spill. He did not see much formalization of the lessons learned part of the program, especially from an emergency response perspective. From the proactive side, he recommended the use of trial runs. Dr. Mutlu noted that the ECIC program employs what they term "fire drills," where they develop draft plans for emergency response scenarios.

Following up on Dr. Eaton's comments about the moving target, Dr. Gray inquired about how the program's stakeholders were delivering value. She applauded the diversity of the program's stakeholders and requested they include indigenous and Latinx stakeholders, particularly in terms of addressing environmental health disparities. She praised Dr. Fenton's work with the North Carolina PFAS[2] Testing Network as an example of effective involvement with stakeholders. She emphasized the importance of two-way dialogue with stakeholders. Dr. Mutlu said the team has

[2] PFAS = Per- and polyfluoroalkyl substances

recognized that more stakeholders should be involved, particularly with horizon-scanning and scoping activities. Dr. Lunn noted that several projects in the group's pipeline intend to involve stakeholders. Dr. Smith-Roe said that dialogue with stakeholders helps add to understanding about what capabilities can be developed at NTP.

Dr. Russi described how chronic kidney disease of unknown origin has been a vexing epidemiological mystery for decades. He asked whether DNTP is adequately leveraging collaborations with other organizations where there is an emphasis on epidemiology to complement toxicological studies. He also asked whether toxicological studies are being pursued, for example with glyphosate, to examine some of the simultaneous causes that could be involved. Dr. Lunn agreed that there is a need for collaborative studies between epidemiology and toxicology.

6.3.2. Second Question

Consider the Problem Statement, Objectives, and Value Proposition in the Program Concept document:

Share your insights on whether there is sufficient focus to deliver the intended value to stakeholders.

Dr. Eaton commented that it is good to see that there are internal collaborations with other NIEHS programs focused on disaster response. Dr. Fenton described collaborative efforts to map contaminants and historically marginalized communities and the potential to initiate new strategies and conversations.

Dr. Gray said it would be important to include environmental health sciences core centers funded by NIEHS. She suggested that there should be unique sets of stakeholders for individual ECIC projects. Dr. Gray also wondered whether DNTP has considered an environmental justice advisory board, indicating that there seems to be a burden put on each program to consider stakeholders related to environmental justice and health disparities, and that perhaps a higher level of organizational thinking would be useful. She added that it might be possible to work with existing groups elsewhere. Dr. Lunn noted that NIEHS has recently created a cross-disciplinary group for environmental justice and environmental health disparities issues. Dr. Gray replied that it sounded like a good start to addressing the issues.

Dr. Singla asked about the expected outcomes of ECIC projects and whether there would be specific products for individual stakeholders, such as fact sheets or other types of information. Dr. Blystone replied that frequently, and working with Dr. Wolfe's office, the group issues fact sheets and develops websites to add context to technical findings.

Dr. Chiu asked for more insight on how individual projects would be designed. He wondered if it would be possible to develop templates for research designs so that the process would not have to be reinvented with every scoping. Dr. Mutlu referred to the decision framework for the three different approaches—top down, bottom up, and horizon scanning. She agreed that stakeholder endpoints are important for the designs. She provided details about what she described as an iterative process of project design. Dr. Fenton added that with every project there is a project development/study design team, which incorporates the right people to ensure all aspects of the problem are worked out, to include internal and external personnel, and potentially including stakeholders. Dr. Mutlu noted the importance of being able to identify gaps.

Dr. Chiu asked how the stakeholders would determine the right question to ask of NTP. He suggested having vignettes as examples, to give people a framework for thinking about what they might ask for. Dr. Fenton agreed that some situations call for the involvement of other stakeholders and stated that there are capabilities that NTP needs to develop, such as high-throughput testing.

6.3.3. Third Question

Looking ahead, what do you see as the top opportunity or challenge in this Program?

Dr. Mader read the question and asked the board members to provide their individual responses using the MURAL tool. BSC members' written responses from the MURAL activity are provided below (see Attachment B for actual MURAL output). The ECIC program also posed a question directly to the board, noted below and in Attachment B.

- ECIC program: "How do we choose only one or two areas to focus on by using proactive horizon scanning efforts?"
- Dr. Berube: Proactively discerning anticipated events involves a handful of methods which, when used in consort will allow different stakeholding populations to respond comfortably and you may need to be very flexible to designing sets of them for different purposes.
- Dr. Blomme: Ensuring sufficient focus/appropriate prioritization and efficient communication to deliver clear value to various stakeholders.
- Dr. Chiu: Being able to better anticipate what might be needed in the future – so as to enable more rapid response when the need arises.
- Dr. Eaton: Opportunity to use state of the art analyses to identify potentially new chemicals of concern – e.g., National Health and Nutrition Examination Survey (NHANES)-like analyses of human blood – but untargeted, e.g., umbilical cord blood example, especially in underserved populations.
- Dr. Felter: Characterizing/communicating uncertainty (or confidence) associated with new methods needed for rapid responses (emergencies).
- Dr. Gray: Balancing time-sensitivity of necessary analyses with stakeholder engagement across multiple partnering organizations, adequately incorporating environmental health disparities into an already complex frame.
- Dr. Martin: Opportunities: Timely impacts using available resources/technologies. Challenges: Having those resources and capabilities available and ready to be deployed.
- Dr. Payne-Sturges: Exposure concerns of tribal communities. Opportunity to link with White House Environmental Justice Council, leverage exposome data from NIEHS funded researchers and NHANES to identify exposure disparities as input to horizon scanning activity.
- Dr. Russi: Establishing adequate experimental test systems for the evaluation of diseases arising out of a multiplicity of factors, many non-toxicological.

- Dr. Anne Ryan: Demonstrating near term impact to influence policy and/or regulatory decision making; are resources "ring-fenced" for those "drop-in" emergencies or are things reprioritized?
- Dr. Singla: Categories of ECICs (1. known contaminant, little data; 2. known contaminant, lots of data but new concern(s); 3. emergent health issue) – each category requires unique capabilities. Identify capabilities needed for each, then evaluate where there may be gaps. Prioritize focus area to fill gap(s).
- Dr. Tilton: Opportunity: Prioritizing projects based on health disparities and impacted communities. Challenge: Potentially too many projects/options and the need to establish more stringent criteria for decision framework that is unique from other programs.

After all responses were received from the board, ECIC program team members internally discussed the responses while other attendees were on a break. Dr. Mader then reintroduced the ECIC program and invited team members to share their thoughts about the board's responses.

Dr. Mutlu pointed out that the team has discussed many of the same opportunities and challenges. Dr. Blystone observed that prioritization is often a difficult task that involves engagement with stakeholders and internal leadership. It is critical to share information as data is generated, engage in back-and-forth communication with stakeholders, and remember that there is no predetermined path or easy template to follow. Dr. Lunn acknowledged several board member responses referred to health disparities, which fall under the umbrella of prioritization. She noted that there was a growing emphasis that communities should have an input on what environmental contaminants DNTP should be concerned about and described efforts related to the exposome. Dr. Fenton added that she was excited by the opportunities noted by the board, and that the team agrees with them. The team hopes to be more impactful in the area of marginalized communities, particularly areas where there is a very specific issue. Dr. Smith-Roe commented that the program is aligned with BSC members in terms of the challenges identified. She asked for more guidance from the board regarding prioritization.

Dr. Gray noted that, given the complexity of what is being done by the team and its responsive nature, it is important to be transparent about the decision-making process, including how and where that information will be posted. Dr. Blystone agreed, noting that in the past, the team has published website updates to provide information to the various stakeholders.

Dr. Berube mentioned that determining how to establish priorities would be a big challenge, because public priorities are not scientific priorities. Dr. Fenton asked Dr. Berube for advice on horizon scanning, and particularly how to choose one or two focus areas. He replied that it must be thought through ahead of time because it is difficult to fix once you start going down the wrong trail. Dr. Eaton added that it is challenging to manage expectations when there is a situation in which a priority has been identified only to have a situation emerge that changes the outlook. As an example, Dr. Fenton discussed previous comments regarding cleaning products.

7. Adjournment

Dr. Berridge thanked the BSC members for their valuable time and feedback and the DNTP staff for their energy and engagement. He felt that once all teams have presented, it would be useful to meet to pull together the various elements, including recurring themes. The synergies amongst

the teams' proposals, and how they are integrated and executed, will allow NTP to achieve the breadth of impact represented by the teams.

Dr. Scruggs added her thanks to the board and to Dr. Eaton for his able chairing of the meeting. She noted that a survey would be going out to the board to gather its valuable feedback.

Dr. Eaton thanked the DNTP teams that presented at the meeting and adjourned the meeting at 4:49 PM.

8. Approval of the Summary Minutes by the NTP BSC Chair

These summary minutes have been read and approved by the chair of the April 23, 2021 NTP Board of Scientific Counselors.

David Eaton, PhD, University of Washington

NTP BSC Chair

Date: June 25, 2021

9. Attachments

Attachment A

Occupational and Inhalation Exposures Program

Looking ahead, what do you see as the top opportunity or challenge in this Program?

David Berube

This is a remarkable program that will be challenged as the stakeholder population diversifies. Developing protocols for just such an occasion would be a good tool.

Eric Blomme

Validation of new proposed in vitro models, including understanding of translatability to humans and of performance characteristics

Weihsueh Chiu

Prioritizing among the many potential inhalation toxicants to maximum public health impact.

David Eaton

Interfacing with NIOSH and industry to obtain 'real world' exposure levels that can help to design human-relevant in vitro and in vivo studies

Susan Felter

Inhalation models that address complex human exposure scenarios, including short-term, intermittent

Kathleen Gray

Engaging effectively with non-federal (and non-industry?) stakeholders

Matthew Martin

Balancing assessment of high priority occupational or inhalation toxicants while evaluating and advancing next generation approaches like MPS and RWD

Devon Payne-Sturges

Chemical and non-chemical exposures in the workplace and their synergistic effects; increase in use of cleaning products due to COVID, including inside schools

Mark Russi

Adequacy of animal and in vitro models to reflect dysfunctional immune responses

Anne Ryan

Balanced portfolio (concept->communication) with operational efficiency and speed to stakeholders; assess impact of data reported-does it result in changes in exposure?

Veena Singla

Ensure data are informing mitigation of health risks

Susan Tilton

Opportunities for non-occupational exposures / stakeholders

Attachment B

Emerging Contaminants and Issues of Concern Program

Looking ahead, what do you see as the top opportunity or challenge in this Program?

Program Management Team

How do we choose only one or two areas to focus on by using proactive horizon scanning efforts?

David Berube

Proactively discerning anticipated events involves a handful of methods which when used in consort will allow different stakeholding populations to respond comfortably and you may need to be very flexible in designing sets of them for different purposes.

Eric Blomme

Ensuring sufficient focus/ appropriate prioritization and efficient communication to deliver clear value to various stakeholders

Weihsueh Chiu

Being able to better anticipate what might be needed in the future - so as to enable more rapid response when the need arrises

David Eaton

Opportunity to use state of the art anlyses to identify potentially new CoC - e.g., NHANES like analyses of human blood - but untargeted. e.g., Umbilical cord blood example, especially in underserved populations

Susan Felter

Characterizing/communicating uncertainty (or confidence) associated with new methods needed for rapid responses (emergencies)

Kathleen Gray

Balancing time-sensitivity of necessary analyses with stakeholder engagement across multiple partnering organizations; adequately incorporating env. health disparities into an already complex frame

Matthew Martin

Opp: Timely impacts using available resources/ technologies. Challenges: Having those resources and capabilities available and ready to be deployed

Devon Payne-Sturges

Exposure concerns of tribal communities; Opportunity to link with White House EJ Council; leverage exposome data from NIEHS funded researchers and NHANES to id exposure disparities as input to horizon scanning activity

Mark Russi

Establishing adequate experimental test systems for the evaluation of diseases arising out of a multiplicity of factors, many non toxicological

Anne Ryan

demonstrating near term impact to influence policy and/or regulatory decision making;? are resouces "ring-fenced" for those "drop -in" emergencies or are things reprioritized?

Veena Singla

Categories of ECICs (1. known contaminant, little data; 2. known contaminant, lots of data but new concern(s) 3. emergent health issue)- each category requires unique capabilities. Identify capabilities needed for each, then evaluate where there may be gaps. Prioritize focus area to fill gap(s).

Susan Tilton

Opportunity: Prioritizing projects based on health disparities and impacted communities; Challenge: Potentially too many projects/options and the need to establish more stringent criteria for decision framework that is unique from other programs