National Toxicology Program

Board of Scientific Counselors

December 8, 2021

National Institute of Environmental Health Sciences
Research Triangle Park, NC

Summary Minutes

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1. Location of Background Materials, Written Public Comments, and Presentations

Background materials, written public comments, and presentations for the December 8, 2021 Board of Scientific Counselors meeting are available on the National Toxicology Program (NTP) Past BSC Meetings page (https://ntp.niehs.nih.gov/go/meeting)

2. Abbreviations and Acronyms

AAAS	American Association for the Advancement of Science
BSC	Board of Scientific Counselors
CV	Cardiovascular
DNTP	Division of the National Toxicology Program
HIV	Human immunodeficiency virus
NICEATM	NTP Interagency Center for the Evaluation of Alternative Toxicological Methods
NIEHS	National Institute of Environmental Health Sciences
NIH	National Institute of Health
NTP	National Toxicology Program
SDOH	Social determinants of health

3. 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
Weihsueh Chiu, PhD, Texas A&M University
Susan Felter, PhD, Procter & Gamble
Kathleen Gray, PhD, University of North Carolina, Chapel Hill
Pamela Lein, PhD, University of California, Davis
Matthew Martin, PhD, Pfizer, Inc.
Devon Payne-Sturges, DrPH, University of Maryland, College Park
Mark Russi, MD, Yale University
Anne Ryan, DVM, PhD, Act 5 Ventures, LLC
Veena Singla, PhD, Natural Resources Defense Council
Susan Tilton, PhD, Oregon State University

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

Rick Woychik

[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 not listed.

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

Brian Berridge
Scott Masten
Mary Wolfe

Other Federal Agency Staff

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

Contract Support Staff

Sarah Colley, ICF
Ernie Hood, Bridport Services
Jeanne Luh, ICF
June Mader, GOFORWARDLLC
Samantha Snow, ICF
Leah West, ICF

4. Introductions and Welcome

The National Toxicology Program (NTP) convened a meeting of its Board of Scientific Counselors (BSC) on December 8, 2021, via Zoom for identified attendees noted above and webcast for public attendees. Dr. David Eaton served as chair. Dr. Mary Wolfe 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, Mary Wolfe, Gonçalo Gamboa da Costa, and Brian Curwin to introduce themselves. Dr. Wolfe read the conflict-of-interest policy statement and briefed the attendees on meeting logistics.

5. 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.

After reviewing the agendas from the 2020 and 2021 BSC meetings, which focused on introducing DNTP programs categorized by strategic areas of focus, Dr. Berridge outlined the purpose of the current meeting, including presentations on the state of the DNTP, the DNPT strategic portfolio, looking forward into 2022 and beyond, and how the board has influenced DNTP's future directions.

There were no clarifying questions from the BSC members.

6. Public Comments

Dr. Eaton noted that the board received two written public comments, one from Stewart E. Holm, chief scientist at the American Forest & Paper Association and American Wood Council, and one from Lindsay Marshall, biomedical science advisor at the Humane Society of the United States and Gillian Lyons, director of regulatory affairs federal affairs at the Humane Society Legislative Fund.

There were no requests to present oral public comments.

7. State of the DNTP FY 2021

Dr. Berridge briefed the board on DNTP's many accomplishments in FY 2021. His aims were to:

- Reflect on exemplary accomplishments over the past year and create a broader visibility for the breadth of what DNTP does.
- Recognize how individual efforts and accomplishments align to the DNTP Strategic Realignment and the recently introduced DNTP Strategic Priorities.
- Get BSC feedback on the DNTP "State of the Union" and input on the division's future.

The DNTP research portfolio has been organized using a strategic framework based on three objectives:

- Accelerate DNTP progress toward becoming a more predictive, precise, and preventive science through the deliberate application of a translational toxicology pipeline of capabilities.
- Provide an evidence-based approach to identify and understand potential environmental contributors to contemporary and common diseases.
- Improve DNTP's ability to conduct and communicate substance-based hazard evaluations that are more translational, innovative, and responsive.

Four strategic areas of focus for the DNTP research portfolio were identified, with webpages for each available on the National Institute of Environmental Health Sciences (NIEHS) website[2]. To implement the strategic framework, Dr. Berridge described several actions that are currently underway as well as others scheduled for 2022, including Portfolio Review 3.0 and BSC engagements on cross-cutting topics. He reviewed DNTP engagement with the BSC over the past year.

Turning to DNTP accomplishments in FY2021, Dr. Berridge provided data for publications, public health impacts, media attention, and NTP website activity. DNTP had 146 scientific publications on a wide variety of topics. He summarized the impact of work by DNTP and the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), including outreach through webinars and workshops. Dr. Berridge then described media mention and stories related to bisphenol A, fluoride, and the Report on Carcinogens. NTP webpages were viewed approximately one million times, with approximately 1.6 million items downloaded.

During the past year, DNTP improved reporting, peer review, and research portfolio governance processes and enhanced project management. The division also addressed work-life balance through changes in practices, new guidelines for effective working, and input into larger institute efforts.

In summary, Dr. Berridge noted that:

- DNTP has continued to be productive and impactful under extraordinary circumstances.
- Change and resilience have become part of the fabric of DNTP.
- DNTP continues to focus on priorities and innovating the future despite the complexity of DNTP pipelines and the uncertainties of the current physical workspace.
- DNTP remains a model for what an effective research organization looks like in the 21st century.

Clarifying Questions

In response to a clarifying question from Dr. Eric Blomme, Dr. Berridge commented that digital pathology has had a significant effect on the DNTP Pathology Working Groups, which are currently being conducted remotely via digital imaging due to the pandemic. It allows for a much more efficient engagement of a broader group of reviewers than in the past. Also, it facilitates the ability to incorporate more artificial intelligence and machine learning into pathology. Dr.

[2] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/index.cfm

Berridge indicated that he would like to see pathology be more quantitative, increasing its ability to be integrated with other types of data.

Dr. Pamela Lein suggested that BSC meetings adopt a hybrid approach, continuing with quarterly virtual meetings but gathering once a year in person. She asked Dr. Berridge about DNTP staff reactions to the state of the union address and where training fits into DNTP's strategic plan. Dr. Berridge commented that the feedback from DNTP staff was characterized by pride, recognizing the significant impact and productivity of the organization. He noted that the staff presentation included more information on training as that is seen as a very important part of DNTP's mission, as evidenced by increasing investment in training fellowships and development of a formal pathology curriculum.

Dr. Eaton brought up the move toward letter review versus committee review, commenting that in his experience he found the face-to-face interaction of committee members to be hugely informative, resulting in a more robust report. He encouraged a return to the committee reviews if possible. Dr. Berridge agreed and said DNTP is working to be judicious in its practices, using letter review for products with limited or no findings and using committee review for more critically important products.

Dr. David Berube noted that he and his colleagues are starting to collect data on how effective virtual meetings are versus in-person, face-to-face gatherings. Initial data is shedding light on problems with attention, retention, and analytic thinking during virtual meetings. He mentioned a study from Stanford[3] and said there would soon be a data-rich environment showing that there could be some serious long-term implications from Zoom and other videoconferencing platforms. Dr. Berridge said that it will be important to look at the data critically when it becomes available and be smart in the use of videoconferencing rather than always defaulting to in-person interactions.

Dr. Matthew Martin asked Dr. Berridge for his thoughts regarding internal training versus strategic hiring or outsourcing in areas such as digital pathology and computational biology. Dr. Berridge replied that the approach is ultimately strategic. While there is opportunity to learn basic principles for more effective engagement with data scientists, the desire is to allow for interdisciplinary and multidisciplinary engagement of people to stretch themselves. Strategic hires, in keeping with the pace of development, will be part of the approach. In some cases, external collaborations will make more sense than hiring.

Dr. Weihsueh Chiu commented on Zoom fatigue. He said that an approach taken by some National Academies committees has been to pre-record the presentations and have people view them prior to attending the meeting itself, with most of the meeting time focused on discussion. Dr. Berube said that the American Association for the Advancement of Science (AAAS) and some of the other science communication groups have adopted that model and have found that it reduces Zoom fatigue. Dr. Woychik added that the model has been used for BSC reviews of the Division of Intramural Research programs. Dr. Berridge agreed that it would be part of the effort to maximize balance between formality of presentations and interpersonal interaction. Dr. Woychik further commented that feedback from the most recent BSC program review suggested that some of the dynamics of the meeting were lost without full presentations. Dr. Berridge

[3] Rabindra R., Miller, D.B., Bailenson, J.N. (2021) Cyberpsychology, Behavior, and Social Networking. Published online: Nov 25, 2021. http://doi.org/10.1089/cyber.2021.0112

suggested that another approach might be to pre-record full presentations but play short vignette summaries during the meeting itself.

7.1. BSC Discussion

Dr. Eaton presented the board the following topic for discussion:

> ***Now that you have heard about our impact, please share your best practices about performance metrics. What can we apply here?***

Dr. Berridge added, "What are we not measuring that we should be?"

Dr. Eaton said that since he had been on the BSC, he had not seen much discussion from the board about major conclusions or controversies that have come out of reviews of DNTP scientific reports. He gave the example of the fluoride report that Dr. Berridge discussed during his presentation. More education on those aspects would be useful for the board.

Dr. Lein noted that tracking training success would be important going forward, and that there are several existing metrics that could be used to track the impact of DNTP training efforts. She also suggested tracking how successfully DNTP-developed technologies and models are being adopted by the greater scientific community. Dr. Berridge cited the examples of NICEATM's tracking of successful adoption of alternative methods and measuring hit rates on the web.

Dr. Blomme mentioned that in pharma there is always a struggle to provide a visible career path for top scientists. He noted that being a leader in the field does not just involve good management, but also requires creating an environment that drives and supports the visibility of the science. He asked Dr. Berridge about his philosophy on that issue. Dr. Berridge indicated that while the traditional National Institute of Health (NIH) system is geared toward a principal investigator approach, that is not the way DNTP operates, so it is sometimes difficult for DNTP scientists to fit into the NIH model and advance. He described efforts on a new approach to better recognize and provide opportunity for scientific leadership within the DNTP multidisciplinary model with more emphasis on team leadership, program leadership, and project leadership. Formalizing leadership of project teams will be a basis for consideration of career advancement and promotions.

Dr. Anne Ryan commented that a strength of DNTP is addressing previously intractable toxicological questions and suggested developing metrics to capture translation, predictivity of some of the newer assays, and timeliness of the work.

Dr. Kathleen Gray remarked that there is an opportunity to streamline stakeholder engagement and engage more with socially and economically marginalized communities, who face higher barriers to participation. She suggested identifying groups who may be missing in DNTP stakeholder engagement processes and then tracking engagement with those groups. Dr. Berridge appreciated the comment and suggestion and noted that DNTP is highly committed to engaging with those communities.

Dr. Devon Payne-Sturges was particularly struck by Dr. Berridge's slide on who was using DNTP materials. She thought it would be interesting to contextualize that information more, especially in considering circumstances under which certain groups use DNTP materials. Dr. Wolfe said that tools to assess and contextualize the effectiveness of DNTP work are being developed.

Dr. Woychik asked BSC members whether they felt that the current approach of DNTP was a slight tweak on past approaches, a 1 on a 10-point scale, or a 10, a major departure away from past practices. Dr. Eaton said it was "up there," but it was a hard question to answer because he did not have enough direct experience with the inner workings of DNTP prior to Dr. Berridge's tenure. He had seen substantial improvements and change in the organization under Dr. Berridge's leadership. Dr. Berridge said that DNTP has attempted to build upon past strengths and refine approaches. Dr. Chiu felt that DNTP is still in a transitional period, with some past elements winding down while new approaches are being developed and set up. Dr. Martin agreed that there is a directional transition focused on moving toward a more disease-oriented approach, which could lead to similar work aimed differently or very different work. He advocated for a greater focus on classes of chemicals instead of individual compounds and emphasis on disease relevance with clinically translatable components. He approved the technological developments taking place. Dr. Berube suggested a brainstorming session to generate endpoints and metrics that would be consistent with the DNTP mission, with a subsequent cost/benefit analysis on whether the endpoints are worthwhile to pursue. Dr. Susan Felter said she had seen tremendous evolution in DNTP goals and focuses as a long-time consumer of the group's work in carcinogenesis. She highlighted the translational aspect of going beyond the rodent bioassay to more information on the impact on human health. She underscored NTPs commitment to better understand how toxicological data can be used in protecting human health.

8. DNTP Strategic Portfolio

Dr. Scott Masten, Director of the DNTP Office of Portfolio Strategy, briefed the board on the ongoing process of DNTP strategic planning and the structure, planning, and management of DNTP portfolio strategy. He started by reviewing the DNTP goals:

- Collaborate with public stakeholders and global partners to identify and address public health issues.
- Generate and communicate trusted scientific information to support decision-making on environmental hazards of public interest.
- Lead the transformation of toxicology through the development and application of innovative tools and strategies.
- Educate and train the next generation of translational scientists to be innovative leaders in the field.

Dr. Masten revisited the three strategic objectives previously described by Dr. Berridge and outlined the four strategic areas of focus and ten DNTP Research Programs:

- Exposure-based Research Programs (Combined Exposures and Mixtures, Consumer Products and Therapeutics, Occupational and Inhalation Exposures).
- Responsive Research Programs (Emerging Contaminants and Issues of Concern, Safe and Sustainable Alternatives).
- Health Effects Innovation Programs (Carcinogenesis, Cardiovascular [CV], Developmental Neurotoxicity).

- Strengthening Capabilities Programs (Novel Tools and Approaches, Scientific Cyberinfrastructure).

Strategic priorities were determined based upon opportunity for impact, availability of resources, and ability to execute. The priorities have also been influenced by cross-cutting topics and BSC input, such as output and outcome metrics; equity, diversity, and inclusion; capability building for the future; and optimizing stakeholder engagement and communication.

Dr. Masten reviewed the program research priorities related to the three strategic objectives as well as thematic research priorities, which were identified as high-value opportunities to strategically implement contemporary and/or cross-cutting topics across all research programs. Elaborating on the thematic research priorities, Dr. Masten described several DNTP projects relevant to social determinants of health (SDOH) and research on the impact of climate change on human health. He discussed the many DNTP stakeholders with diverse roles and relationships.

Dr. Masten concluded by providing a summary of the key points:

- The DNTP research portfolio is organized around overarching strategic objectives.
- Individual research programs align to those objectives while tackling important opportunities in DNTP's mission space.
- Strategic research priorities will guide focused effort over the next 3 years, delivered by executing projects from across all programs.
- The DNTP strategy and operational model affords flexibility to apply resources and areas of strength to address timely and important public health issues.
- Stakeholder interests and needs drive the work of DNTP; establishing and nurturing these interactions at scale requires creative approaches.
- DNTP knowledge products effectively reach traditional scientific and regulatory audiences; much greater impact could be realized by developing novel outputs.

Clarifying Questions

Dr. Eaton asked how hazard and exposure assessment are brought together to address risk in the example of personal care products, noting that stakeholder engagement could be really useful. Dr. Masten replied that although DNTP does not do formal risk analysis, it can address relative safety and work directly with interested stakeholders to understand what information they are looking for. Dr. Eaton agreed that the distinction between hazard and risk is important.

Dr. Blomme asked how the prioritization process would work within the shared resource model. Dr. Masten stated that what is often rate-limiting for DNTP is people power. Prioritization then stems from who is available to work on a given project, and through that some prioritization issues tend to work themselves out.

8.1. BSC Discussion

Dr. Eaton introduced Dr. June Mader, who facilitated the board's discussion of three questions intended to focus on DNTP impact and relevance to emerging public health issues:

1. How should DNTP refine toxicology study and assessment approaches to better understand and account for social determinants of health?

2. How should DNTP selectively adapt current projects to address the disproportionate impacts of climate change on individuals and populations?

3. How should DNTP define creative approaches to effectively engage stakeholders to increase the impact of DNTP research products?

The board broke into three groups to discuss the questions while other attendees were on a break. Each breakout group was asked to consider the three questions from the perspective of decision makers, concerned citizens, or the scientific community. One member from each group then reported on their discussions.

8.1.1. Group 1: Decision Makers

Dr. Chiu reported on Group 1's discussion, taking the role of "Decision Makers" (see Attachment A for slides presented).

On Question #1, the group suggested adapting systematic evidence mapping or systematic review approaches to look at other types of exposures related to SDOH. There are several issues with trying to experimentally model SDOH that will require novel approaches to address. Another possible direction for DNTP to explore might be interactions between social determinants and toxic exposures. The group's discussion focused on the need to identify place-based vulnerabilities.

On Question #2, the group recommended emphasizing exposures that will likely change during climate change, such as air pollution from increased wildfires and heat stress from increased temperatures. Another area that could be adapted is the interaction of infectious diseases or toxic substances with immunotoxicity. Dr. Chiu noted that the CV program would be another major area for consideration.

On Question #3, the discussions arrived at two main points: first, training and engaging stakeholders in the use of the research products; second, making the information accessible to inform clear decisions by the wide range of stakeholders in decision-making roles. Dr. Chiu mentioned several specific suggestions for making information accessible, such as fact sheets, graphics, visualizations, and data dashboards that are fit-for-purpose for different audiences.

8.1.2. Group 2: Concerned Citizens

Dr. Gray reported on Group 2's discussion, taking the role of "Concerned Citizens" (see Attachment B for slides presented). She noted that the group began their discussion by debating the question itself, as "concerned citizens" is a broad, general category. They chose to pursue the questions from the perspective of advocacy groups or geographic communities that may be socially or economically marginalized.

On Question #1, concerned citizens would want to know that *in vivo*/*in vitro* studies would reflect a range of populations, so that they could have confidence that their unique exposures, life experiences, and stressors were taken into account as much as possible in study parameters. The group discussed the need to be clear about what determinants of health are being considered in any studies.

On Question #2, the group was challenged to think about whether concerned citizens are aware of research efforts related to climate change that are happening within DNTP. Dr. Gray noted that NIEHS is connected to community-based organizations working on climate change issues. These organizations would be in the best position to comment on how DNTP research projects could be adapted. An interesting space for DNTP is the intersection of disease outcomes and vulnerable populations, such as farmworkers and heat stress as well as pesticide exposures.

On Question #3, the group felt that DNTP needs to be strategic rather than creative in engaging stakeholders. DNTP has done a great job with scientists and decision makers, but there are limited resources for every team to reach concerned citizen groups. Therefore, an analysis of who DNTP most wants to engage and how it can be done strategically is warranted.

8.1.3. Group 3: Scientific Community

Dr. Lein reported on Group 3's discussion, taking the role of "Scientific Community" (see Attachment C for slides).

On Question #1, the group wondered how underlying conditions affect response. Is it related just to the amount and type of exposure, or is it related to biological differences because of social disadvantages? It seems that DNTP may be able to refine some of its ongoing projects to start to get at some of those interactions. Discussions also considered exploring the mechanisms of how stressors influence disease, either onset or progression, as well as response to toxic exposure. It is difficult to understand how new approach methodologies might apply to understanding very complex interactions involving multiple physiological systems. DNTP might be uniquely positioned to address the question of whether stress biomarkers in humans are representative of biomarkers in animals.

On Question #2, Dr. Lein said the group noted the renewed emphasis on exposures. There is an opportunity for DNTP to have positive impacts on understanding the impact of climate change in the context of wildfire/urban interfaces, where there is currently little data on the toxic components that are derived from the burning of the built structure. They recommended getting a better handle on exposure to mycotoxins because of the important role temperature and humidity have on mycotoxin contamination of certain crops. The group commented that of the various health effects innovations programs within DNTP, Cardiovascular and Developmental Neurotoxicity seem well positioned to start integrating climate change issues. They also discussed developing a mechanistic understanding of how increased exposure to environmental pollutants is impacting physiologic systems and how heat stress influences the response to environmental exposures.

On Question #3, DNTP should consider how to position the timing and coordination of releases of DNTP scientific reports to have the biggest impact on the scientific community. The group recommended thinking about the scientific community as an active co-author, not just an end user, in preparing reports. By identifying relevant stakeholders during report preparation, the message could be refined in terms of the stakeholders. The group identified the challenge of engaging industry stakeholders without introducing conflicts of interest. Industry holds vast amounts of data that are not available for public consumption and that may be extremely useful. Opening the resource prioritization conversation to the public to facilitate access to industry data without raising conflicts may be a worthwhile effort. Development of a public clearing house for unpublished or raw data would be a huge boon to the scientific community for understanding

some of the complex environmental health issues that may be related to exposures to proprietary products. The group recommended pursuing other methods of establishing scientific partnerships beyond interpersonal relationships, such as program announcements to attract partnerships that may not have been readily apparent.

9. Looking Forward: Innovation in the NIEHS Division of the National Toxicology Program

Dr. Berridge proposed innovation as a theme for DNTP going forward. He noted that innovation is not a new concept for DNTP, but there is a firm foundation of innovation within the division, so the organization is truly building on historic strengths. There is a commitment to lead the transformation of toxicology through the development and application of innovative tools and strategies. Innovation is a core value and strength of DNTP.

To illustrate the concept of continuous improvement, Dr. Berridge provided several examples of recent innovations within the organization, affecting nearly every office and branch. He described an updated version of the Translational Toxicology Pipeline for 2021. Human health effects are featured in the newer version as the organization evolves to incorporate human studies in its scientific pursuits. He noted advances in evidence informatics and ways in which DNTP hopes to leverage informatics to support evidence-based decisions:

- Identify, adapt, and develop a toolbox of informatics approaches to advance DNTP's ability to turn data into knowledge for understanding human health effects from environmental exposures.
- Improve workflow, reduce manual workload, and identify tools for the range of DNTP users.
- Support synthesis through identification and categorization to better link mechanism to experimental and epidemiological data.

DNTP innovations also include systems-based high-throughput screening, CV-relevant bioactivity targets, and application of complex *in vitro* systems, including several *in vitro* models of human disease. He discussed a computationally oriented future with rapidly advancing abilities to not only generate data but to integrate it and generate new knowledge from it as well. Dr. Berridge further noted the development of multiscale modeling and the need to enter into partnerships to help facilitate the maturation of the field and development of new computational tools.

In looking to the future, Dr. Berridge discussed the concept of integrating subclinical disease into toxicology, citing the work associated with characterizing the cardiovascular health hazards of human immunodeficiency virus (HIV) therapeutics. There is also interest in exploring the role of genetic susceptibility in the variability of exposure responses and in the use of integrative physiological monitoring in animal studies. Dr. Berridge reported that artificial intelligence is now routinely used in toxicological pathology. He also described translational human research efforts to link exposures to disease, using biomarkers to understand exposures and predict disease outcomes.

In summary, Dr. Berridge noted that:

- There is a long history of innovation at DNTP. The DNTP has actively and continuously refined organizational processes and structure and has been a leader in developing novel approaches to environmental hazard assessment.
- DNTP significantly increased efforts to innovate the way toxicology is applied in hazard identification and characterization despite the innumerable distractions of the last few years.
    - DNTP embraced the intent to be more predictive and translational.
- All of DNTP's efforts to innovate the operation and execution of its science are aligned to contemporary problems DNTP is trying to solve.
- DNTP looks forward to sharing the outcomes of these efforts as it shares the progress and outcomes of its strategic and prioritized portfolio.

9.1. BSC Discussion

Dr. Eaton expressed his approval of the mechanistic focus of much of DNTP's efforts. He asked for Dr. Berridge's thoughts on mixtures as a challenge for environmental toxicology with huge opportunities. Dr. Berridge responded that DNTP has a specific program area devoted to studies on mixtures, such as per- and polyfluoroalkyl substances. Describing DNTP research on botanicals and cannabinoids, Dr. Berridge indicated that a pipeline of capabilities is needed to address the mixtures challenge. DNTP is on the front end of determining how to address the specific complex problem that mixtures pose.

Dr. Eaton mentioned that biomarkers of effect, adverse outcome pathways, and identifying key events to quantitatively measure are other areas of great opportunity for DNTP. Dr. Berridge commented that the scientific community does need to get better at recognizing proximate biomarkers of a bioactivity or health effect. When you can start associating specific biomarkers with specific bioactivities with specific agents then you can begin to understand the complexity of exposures to mixtures.

10. Adjournment

Dr. Berridge thanked the board for its engagement over the course of the past year's meetings, which have laid the foundation for the next generation of products coming from DNTP. He looked forward to next year's proceedings, which will see data on outcomes of the strategic realignment.

Dr. Wolfe thanked the board for participating in several virtual meetings over the past year and for members' valuable input in the process.

Dr. Eaton adjourned the meeting at 4:48 pm, December 8, 2021.

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

These summary minutes have been read and approved by the chair of the December 8, 2021 NTP Board of Scientific Counselors.

David Eaton, PhD, University of Washington

NTP BSC Chair

Date: 2/27/2022

12. Attachments

DNTP Strategic Portfolio

Group #1: Decision Makers

1. How should DNTP refine toxicology study and assessment approaches to better understand and account for social determinants of health?

- First identify key determinants and then identify areas of high-impact or high-visibility (suggestion of leveraging systematic evidence mapping; importance of transferable tools and approaches for different exposures)
- Need to first understand what has significant impacts on health outcomes (e.g., stress, night shift work, nutrition, social isolation—can these be ethically determined experimentally? What is the role of Zebrafish models or high-throughput models?)
- Need research on biological changes that occur with social determinants.
- The dose must also have relevance to human exposures.

Group #1: Decision Makers

1. How should DNTP refine toxicology study and assessment approaches to better understand and account for social determinants of health?

- Some factors vary generally and broadly interact with toxic exposures; some factors interact with specific agents.
- Need to identify populations that may be impacted by toxic exposures (e.g., geographic areas), identifying place-based vulnerabilities will also help identify factors to consider. Must also think about specific agents and particular vulnerabilities.
- Population and place-based information is critical to decision makers (ask the question "is this relevant to my city/state/jurisdiction?"
- Microbiome endpoints are also of interest—may be relevant to Scientific Community group.

Group #1: Decision Makers

2. How should DNTP selectively adapt current projects to address the disproportionate impact of climate change on individuals and populations?

- Start building in models of how exposures might change with climate change (e.g., wildfires and air pollution). Integrate the time-element and ensure NTP captures the high-end exposures and disproportionate exposures.
- Consider heat stress and direct impacts of heat, whether in vivo or in vitro models.
- Consider changing growth patterns of naturally occurring toxins (e.g., expanding ranges of aflatoxins, protozoan diseases). This could be an area for FDA collaboration. Immunotoxicity could also be an entry-point for this work.

Group #1: Decision Makers

2. How should DNTP selectively adapt current projects to address the disproportionate impact of climate change on individuals and populations?

- Interactions of factors related to climate change/SDOH and consider how to integrate.
- Is there a role for epigenetics? (e.g., studies on environmental stress and multi-generation lineages)
- Consider intersections of cardiovascular disease and climate change (e.g., heat stress, air pollution).
- Reiterate the importance of population and place-based considerations—who is impacted and where will impacts fall?

Group #1: Decision Makers

3. How should DNTP define creative approaches to effectively engage stakeholders to increase the impact of DNTP research products?

- Question from the group: does this relate to increase visibility and usage of output?
  - Could relate to building visibility/influence and creating high-value career paths at NTP
- Training remains a critical area—training will aid with adaptation of NTP products
  - (e.g., raw toxicogenomic data can be helpful to wide variety of stakeholders, but how to ensure it is usable and not a 'black box'? NTP must also ensure products are not used inappropriately or premature conclusions are drawn).
  - Previous report on usage of TG data—this could be continuously updated and built upon.
- Can draw insights from the large-scale databases that are already available. NTP can demonstrate leadership in data usage.
- Leverage outside expertise

Group #1: Decision Makers

3. How should DNTP define creative approaches to effectively engage stakeholders to increase the impact of DNTP research products?

- What information is needed to inform the specific decisions in front of a decision maker?
  - Decision makers often do not use raw data (i.e., policy-makers), NTP should better understand how their products are used by decision makers and understand the decisions to be made. NTP should consider how to package products in the most easily usable way. e.g., summaries, fact-sheets, etc. that can accompany monographs or reports that can help fill gaps
  - Risk managers may not use raw data, but risk assessors would use raw data—consider that different stakeholders can communicate effectively about the data.
  - Certain decision makers *do* use raw data (e.g., Dr. Susan Felter and Dr. Eric Blomme use raw data in their own roles as decision makers).
  - Early conversations about these topics are extremely helpful and end products/stakeholders should be considered as early as research design phase.

Group #1: Decision Makers

3. How should DNTP define creative approaches to effectively engage stakeholders to increase the impact of DNTP research products?

- Multiple references to the Scientific Cyberinfrastructure program and the importance of data dashboards and thoughtful packaging of information products. Graphics, visualizations etc. that are fit-for-purpose for different audiences.

Attachment B

Group #2: Concerned Citizens

1. How should DNTP refine toxicology study and assessment approaches to better understand and account for social determinants of health?

- Want to know that the in vitro/ in vivo study design reflects studies considering range of populations affected by exposures, exposures to mixtures/complex exposures – current study design is much straighter
  - Areas of study design: disease
- Organic engagement – meet with groups whose voices have not been engaged
- To what extent is social determinants of health being looked at in terms of exposure?
- Concerned about how the information will be utilized and translated to inform decision-making
- How to reconcile this interest with the push to rely less on animal studies

Group #2: Concerned Citizens

2. How should DNTP selectively adapt current projects to address the disproportionate impact of climate change on individuals and populations?

- Look at where climate change is having the greatest health impact (cardiovascular risk)
- Marginalized populations often have issues because of location (flood plains)
  - Combined effects of heat exposure
  - Pesticides
- How they view current projects intersecting with climate change
- Women in lower socio-economics groups have less access to prenatal care, children are more vulnerable
- NIEHS, through grantees, is connected to concerned citizens who are addressing climate change

Group #2: Concerned Citizens

3. How should DNTP define creative approaches to effectively engage stakeholders to increase the impact of DNTP research products?

- Important to recognize stakeholder engagement
- Highly technical academic style communication is problematic – the public does not evaluate toxicology like scientists
- Who might be the best stakeholder, from the concerned citizen perspective, in these thematic areas?
- Already sustained approaches and networks to reach concerned citizens
- Citizen data science and challenges

DNTP Strategic Portfolio

Group #3: Scientific Community

1. How should DNTP refine toxicology study and assessment approaches to better understand and account for social determinants of health?

- Differences in response are related to amount/type of exposure as well as biological differences (e.g., underlying health effects, compromised immune systems, etc)
- Underlying nonchemical stress (e.g., diet, psychosocial) and how it alters response to chemical stress
- Mechanistic understanding of how stressors (chemical and nonchemical) influence disease and response to toxic exposure
  - How to approach this using NAMs
- Are biomarkers in humans for stress representative to biomarkers in animals? And how are they mechanistically relevant to physiological response?

Group #3: Scientific Community

2. How should DNTP selectively adapt current projects to address the disproportionate impact of climate change on individuals and populations?

- Incorporate exposure to wildfire/woodsmoke in study designs
  - Characterizing exposures at the wildfire/urban interface
- Exposure assessment of mycotoxins (e.g., algal blooms, dietary mycotoxins [aflatoxins])
  - Is exposure increasing with climate change?
  - Are chronic diseases altered by exposure to mycotoxins?
- How are health effects (e.g., CV, pulmonary, neuro) impacted by climate change?
  - Mechanistic understanding of how exposures impact physiological systems
- How does increased temperature (e.g., heat stress) affect response to environmental exposures?

Group #3: Scientific Community

3. How should DNTP define creative approaches to effectively engage stakeholders to increase the impact of DNTP research products?

- Thinking about timeline of how information is released so it has the most impact
- Engage scientific community during preparation of reports (in how data is interpreted and applied)
  - Identifying relevant stakeholder populations while reports are being developed to distribute information to
- How to engage industry stakeholders without introducing conflicts of interest?
- Open resource prioritization discussions to the public
- Developing a public clearing house for [unpublished/raw] data
- Identifying other pathways for scientific partnerships