

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES**

**MINUTES OF THE ONE HUNDRED FIFTY-SIXTH MEETING OF THE
NATIONAL ADVISORY ENVIRONMENTAL HEALTH SCIENCES COUNCIL**

February 20-21, 2019

The National Advisory Environmental Health Sciences Council convened the open session of its one hundred fifty-sixth regular meeting on February 20-21, 2019 in the Rall Building, Rodbell Auditorium, National Institute of Environmental Health Sciences, Research Triangle Park, NC. The closed session of the meeting was held February 20, 2019.

The meeting was open to the public on February 20, 2019 from 11:00 a.m. to 4:30 p.m. and February 21, 2019 from 8:30 a.m. to 10:30 a.m. In accordance with the provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), the meeting was closed to the public on February 20, 2019 from 8:30 a.m. to 10:45 a.m. for consideration of grant applications. Notice of the meeting was published in the *Federal Register*. Dr. Linda Birnbaum presided as Chair.

Participating Council Members

Habibul Ahsan, MD
Philip Brown, PhD (via WebEx, Thursday only)
William Cibulas, Jr., PhD (*ex officio*) (via WebEx)
José Cordero, MD, MPH
Irasema Coronado, PhD
Gary Ellison, PhD (*ex officio*)
Brenda Eskenazi, PhD (via WebEx)
Shuk-Mei Ho, PhD
Katrina Korfmacher, PhD
Maureen Lichtveld, MD (via WebEx)
José Manautou, PhD
Donna Mendrick, PhD (*ex officio*) (via WebEx)
Edith Parker, DrPH
Brad Racette, MD
Susan Schantz, PhD
Andy Shih, PhD
Patrick Sung, DPhil
Robert Tanguay, PhD
Robert Wright, MD, MPH

NIEHS Staff

Kathy Ahlmark
Janice Allen, PhD
David Balshaw, PhD
Linda Bass, PhD
Bryann Benton (via WebEx, Wednesday only)
Brian Berridge, DVM, PhD
Linda Birnbaum, PhD
Abee Boyles, PhD
John Bucher, PhD
Danielle Carlin, PhD
Toccaro Chamberlain
Jennifer Collins
Gwen Collman, PhD
Sally Darney, PhD
Christie Drew, PhD
Chris Duncan, PhD
Anika Dzierlenga
David Fargo, PhD
Christine Flowers
Amanda Garton
Barbara Gittleman
Kimberly Gray, PhD
Janet Hall, MD, MS
Astrid Haugen
Michelle Heacock, PhD
Heather Henry, PhD
Jon Hollander, PhD
Bonnie Joubert, PhD
Helena Kennedy
Heather Knox
Alfonso Latoni, PhD
Cindy Lawler, PhD
Chris Long
Robbie Majors
J. Patrick Mastin, PhD
Kim McAllister
Steven McCaw
Liz McNair
Sri Nadadur, PhD
Aaron Nicholas (via WebEx, Wednesday only)
Liam O'Fallon
Kristi Pettibone, PhD
Tina Powell
Scott Redman
Ericka Reid, PhD

Les Reinlib, PhD
Carol Schreffler, PhD
Thad Schug, PhD
Dan Shaughnessy, PhD
Varsha Shukla, PhD
Ashley Singh
Spencer Smith
Laura Thomas, PhD
Claudia Thompson, PhD
Brittany Trottier
Steven Tuyishime, PhD
Fred Tyson, PhD
Michelle Victalino
James Williams
Mitch Williams
Leroy Worth, PhD
Rick Woychik, PhD
Demia Wright, MPH
Darryl Zeldin, MD

Members of the Public Present

Maureen Avakian, MDB, Inc.
Megan Avakian, MDB, Inc.
Thomas Clasen, JD, PhD, Emory University
Ernie Hood, Bridport Services, LLC
Michael Phillips, RTI International

I. Call To Order and Opening Remarks

NIEHS/NTP Director and Council Chair Linda Birnbaum, Ph.D., welcomed attendees and called the meeting to order. She noted that Council member Dr. Lauren Zeise and *ex officio* Council members Dr. Della Hann and Dr. Michael Slimak were not able to attend the meeting. She presented retiring Council member Dr. Philip Brown with a certificate of appreciation for his service. She also recognized retiring Council members Dr. Habib Ahsan, who had already received a certificate, and Dr. Brenda Eskenazi, who was attending via WebEx. She asked attendees in the room to introduce themselves. Following the introductions, NIEHS Division of Extramural Research and Training (DERT) Director and Council Executive Secretary Dr. Gwen Collman reviewed meeting logistics, including votes to be taken through the Electronic Council Book.

II. Review of Confidentiality and Conflict of Interest

Designated Federal Official Dr. Collman reviewed the Conflict of Interest and Confidentiality procedures, which had been provided earlier to Council members in written form, and reviewed various other administrative matters.

III. Consideration of September 2018 Meeting Minutes

Approval of the September 2018 meeting minutes was moved and seconded, and Council voted to approve the minutes, with all in favor. Dr. Collman noted the dates of the upcoming Council meetings for members to put on their calendars.

IV. Report of the Director, NIEHS

Dr. Birnbaum briefed Council on Institute developments since the September 2018 Council meeting.

She updated the council on budget and appropriations. She said that the Health and Labor budget was passed on September 28, so the Institute is fully funded through the fiscal year. The new appropriation represents a considerable increase over where it was four years ago, representing a \$24 million increase over the previous year. Superfund also received its first increase in several years, an addition of \$1.6 million to its budget. The annual \$10 million worker training pass-through from the Department of Energy has been renewed. Altogether, the NIEHS appropriation totals approximately \$863 million.

Dr. Birnbaum depicted the important leaders in the 116th Congress who will affect NIEHS and NIH. She described recent Congressional engagements, as well as recent *Friends of NIEHS* activities.

Turning to science advances, Dr. Birnbaum briefly summarized several recent publications by NIEHS/NTP personnel or grantees. She began with two One NIEHS papers. The first was a cohort study on PFAS levels and physiological measures authored by NTP and DIR researchers. The second outlined a new approach to screening for developmental neurotoxicity at NTP. She also highlighted recent publications by DIR, DNTP, and DERT scientists.

Dr. Birnbaum provided Council with an update on NIEHS cohort studies. She noted that environmental epidemiological cohort studies take large amounts of resources to develop, implement, and maintain, with initial results often taking up to 6-7 years. The inherent length of the cohort studies presents challenges to both grantees and to NIEHS. In FY17 and FY18 alone, NIEHS supported the development, study, and/or maintenance of 48 environmental epidemiology studies through 125 grants or projects, ranging in size from 84 to 35,000 subjects. Dr. Birnbaum summarized the EARTH study,

the ELEMENT study, and the New Hampshire Birth Cohort as good examples of important cohort studies. She also mentioned several ongoing large cohort studies supported by DIR.

She summarized several recent awards and recognition given to NIEHS personnel and grantees, including several SOT award recipients.

Dr. Cordero asked Dr. Birnbaum to comment on how the cohort studies connect with the ECHO studies. She said that a number of the birth cohorts are part of ECHO.

Dr. Wright asked whether there are plans to create cohorts around clinical diseases. Dr. Birnbaum replied that NIEHS would certainly be interested in doing so, to assess the impact of the environment on a certain disease state. Dr. Collman said it was a topic that had long been under discussion at the Institute, but the majority of the resources have gone to etiologic questions. She said she would welcome Council's input on how to engage with appropriate scientific societies and clinical groups where there would be an opportunity for a demonstration project. She thought it would be a good topic for discussion at a future Council meeting. Dr. Birnbaum pointed out that there had been some work in the area of infectious disease and environmental susceptibility.

Dr. Eskenazi asked how the data that are being collected through the cohorts can be utilized, perhaps through an intermediary mechanism. Dr. Collman mentioned several potential grant mechanisms.

Dr. Racette noted that with several neurological diseases such as Alzheimers, Parkinson's, and ALS, the environment seems to play a significant role in disease progression. He said that disease progression rates should be a focus of studies in the area.

Dr. Ahsan said that research projects should incorporate some environmental measurement in a cohort or sub-cohort. He suggested that newer cohorts should be centered around healthcare facilities, especially when assessment of clinical outcome is included. His second point was that he was excited to see the plan for a conference on machine learning and artificial intelligence planned for June, as it is such an important area for environmental health research. He suggested sharing data from cohort studies so that it could be mined by machine learning algorithms to answer research questions. Dr. Birnbaum replied that NIEHS has funded some efforts in machine learning and artificial intelligence, but they are areas with much opportunity.

Dr. Brown commented on the disease-based cohorts, citing the opportunity for NIEHS to support pioneering research. He supported the use of small grants for accessing and querying the data from cohorts.

Dr. Ho noted that NIEHS has much opportunity to collaborate with international cohorts. She added that in terms of disease cohorts, it would be important to coordinate with some of the other NIH institutes and centers.

Dr. Korfmacher said that in discussing the maintenance of cohorts, a topic that had been raised at a recent Partnerships in Environmental Public Health meeting was the complexity of report-back.

Dr. Ellison discussed what NCI does with regard to cohort infrastructure. He said that NCI supports the infrastructure of cancer epidemiology cohorts, and that many of them are being enhanced with electronic health records data. He said NCI is encouraging investigators to broadly share those data, including high-quality biospecimens.

V. Household Air Pollution Intervention Network (HAPIN) Trial: objectives, design and formative research results

Thomas Clasen, JD, PhD, from Emory University, briefed the Council on the HAPIN trial, a multi-country randomized controlled trial designed to assess the health impact of cooking with liquefied petroleum gas (LPG) over traditional solid biomass fuels. A total of 3200 pregnant women are being enrolled in rural areas across India, Guatemala, Peru, and Rwanda. They, their newborn child and, in a subset of 800 households, an older adult woman are being followed until the child is one year old. Globally, nearly 3 billion people rely on solid fuels for cooking and heating, and the resulting indoor air pollution accounts for an estimated 1.6 million annual deaths. Previous interventions have provided cleaner biomass cookstoves, but have failed to reduce exposures to levels that produce meaningful health improvements. LPG cookstoves are believed to be the cleanest scalable intervention. Clasen summarized the many challenges involved in designing and implementing a complex public health study in remote areas. It has been in progress for more than two years, but after considerable planning and piloting, active enrollment in HAPIN has begun. The study is on track toward completion within its five-year grant period.

Dr. Parker asked about the intensive behavior change strategies being employed in the study. Dr. Clasen said it could be characterized as an efficacy trial, with a responsibility to get the intervention to the eligible participants and ensure they are using it. He discussed how the issue of stacking was dealt with.

Dr. Birnbaum noted that two of the study sites are in hot climates, while the other two are in cold areas. She asked how the differences were controlled for. Dr. Clasen said there was not as much space heating in the cold climates using the stoves as might be expected.

Dr. Ahsan congratulated Dr. Clasen on the good progress that has been made in “an extremely difficult study.” He noted that in some of the areas, LPG stoves are being rolled out commercially, and that many in the placebo groups would likely adopt them, potentially reducing the power of the study. Dr. Clasen said he was concerned about that issue. He noted that people could not be prevented from adopting a cleaner fuel option. He said that in formulating the research, the team went to places where they felt it would not be a problem in an 18-month follow-up period. He said it was a challenge they had worked to manage by going to remote places and incentivizing the controls with an economic gradient.

Dr. Manautou asked about the ancillary studies listed by Dr. Clasen, and said they would constitute a huge undertaking on top of the main study. He also asked Dr. Clasen to address the issue of the economics involved following the conclusion of the study. Dr. Clasen noted that many of the ancillary studies would be conducted only in one or two of the sites. In terms of the post-study economics, he said he really did not have a good answer. In India, there is a massive rollout of LPG. In Peru, there is a lower subsidy. However, the issue is still a barrier to the base of the pyramid. He was most troubled about Rwanda in terms of the people’s ability to afford the fuel after the end of the study.

Dr. Coronado described a previous study in Sinaloa encouraging women to cook outdoors. She suggested enlisting schools of engineering to develop appropriate technologies to develop better stoves in particular areas. She noted that in Sinaloa, once the LPG subsidy ran out, the people went back to their traditional fuels. She cited another recent study in Alaska. Dr. Clasen said the hope from the HAPIN study is to show that governments that it would be advantageous to make the intervention more accessible and affordable for their people.

Dr. Birnbaum pointed out that at least 16 million Americans cook on wood-burning stoves.

VI. The Role of NIEHS in Supporting Children’s Environmental Health from Centers to Next Steps

Dr. Kimberly Gray provided the Council with an update on Children’s Environmental Health (CEH) at NIEHS, including what is being funded, how CEH science is being funded, the NIEHS and EPA Children’s Environmental Health Centers Program, and where CEH and NIEHS go next.

She provided background information about the current issues related to CEH, including body burden of chemicals; vulnerable populations such as pregnant women, children and preconception; developmental plasticity and windows of susceptibility; and the

overall declining state of children's health today. The extensive NIEHS CEH portfolio includes research on:

- Early life exposures
- Contaminants, including metals, endocrine disrupting chemicals (EDCs), and other pollutants in water, air, food, and consumer products in rural and urban settings
- The relation of early life exposures to autism, cognitive dysfunction, ADHD, asthma, diabetes, and other outcomes
- New research areas such as the microbiome, mitochondrial function, placental epigenetics, and immune dysregulation

Dr. Gray went over the many NIEHS FOAs targeting CEH, with details about the funding by science type, exposure, health outcome, location, and grant mechanism.

She discussed the NIEHS and EPA Children's Environmental Health and Disease Prevention Centers program, which was established in 1998. The overall goal of the program is to establish a national network that fosters communication, innovation, and research excellence in Children's Environmental Health with the ultimate goal of reducing the burden of morbidity among children as a result of exposure to harmful environmental contaminants. The centers' purposes are to:

- Promote multidisciplinary interactions
- Accelerate translation
- Cross-foster collaboration
- Provide a forum for community outreach and translation

Dr. Gray described the history of the centers program, and provided an overview of the diverse research being conducted. She listed the current and former centers, and several examples of recent scientific findings. She also discussed several examples of outreach and engagement by the centers, as well as examples of public awareness and education activities. She also mentioned several examples of the program's contributions to early career development, as it is dedicated to training new scientists in the field.

She provided an overview of a translational framework for the centers program, flowing from fundamental questions through to impact. The full framework lists several elements in concentric circles, from initial observation to tangible changes in outcomes. She illustrated the concept with several examples from center research that have had real-world impact

(<https://www.niehs.nih.gov/research/programs/translational/framework-details/index.cfm>).

Dr. Gray concluded with a summary of considerations and opportunities in NIEHS CEH.

- How should we continue to protect our children from environmental hazards?
 - Interdisciplinary research
 - Faculty development
 - Community engagement
 - Translation of the science
- What are some new ways to sustain and integrate the collaborative network of CEH researchers?
- How do we nurture the base and promote the translation of all the CEH science?

Dr. Cordero said it is really remarkable what the organized set of centers can do, and the impact that they are having is tremendous. He asked Dr. Gray to comment on the future of the partnership between NIEHS and EPA. Dr. Gray said that it was difficult at this point in time to anticipate whether we would continue due to restructuring currently underway at EPA.

Dr. Schantz said she appreciated the opportunity to have been involved in the Centers program. Her group does mechanistic studies in animal models, and the ability to pair that research with the human birth cohort has been rewarding.

Dr. Shih said he was particularly impressed with the program's ability to translate findings into policy. He asked Dr. Gray if advocacy was a required element of the program. She replied that community engagement was a required element, with every center managing their community engagement in different ways. Dr. Shih asked if advocacy is built in the program or comes out the results. Dr. Gray said that it comes from the results.

Dr. Wright said that CEH is not taught in medical schools, and wondered if grants to get CEH into medical education might be part of future directions for the program, as a way to get the information into clinical medicine. Dr. Gray said that was a good idea, and that the program does have some activities in that direction.

Dr. Eskenazi, commenting as one of the first center directors, said that historically there had been resistance to the concept of community outreach, but the centers program forced community outreach and translation, and as a result, "I think it has been a magnificent contribution." She noted that the centers program provides funding for the community outreach, which is not seen elsewhere. She felt that that was a real strength of the program, and should continue.

Dr. Ellison asked how much the centers are engaging and empowering the children themselves. Dr. Gray cited the example of USC engaging the Latino youth, and noted that several centers have Youth Advisory Boards.

VII. NIEHS Undergraduate Research Education Program (UP) to Enhance Diversity in the Environmental Health Sciences (R25)

Astrid Haugen from the Genes, Environment and Health Branch presented the NIEHS R25 Undergraduate Research Education Program (UP) in the Environmental Health Sciences (RFA-ES-14-004) to the Council for concept clearance.

The UP program is a key activity in the implementation of the NIEHS Strategic Plan designed to increase the pool of scientists from underrepresented backgrounds engaged in NIH-funded environmental health science research. It provides support to appointed students from underrepresented backgrounds for up to two years of their undergraduate education, typically beginning as rising juniors, to gain hands-on experience with research activities in the environmental health sciences.

The undergraduate student participants in the R25 UP program can be supported for:

- 40 hours per week during the summer
- Up to 15 hours per week during the academic year
- Up to two years

Ms. Haugen provided information about the existing UP programs and the evaluation plans for tracking student success.

The original RFA was released in May 2014, with program funding for five years beginning in April 2015. Council was asked to approve a follow-up funding opportunity to enable the continuation of this undergraduate diversity training program for five more years. Upon approval, the renewed RFA would be targeted for release in May 2019.

Dr. Manautou was the first Council reviewer. He said that although the program gives preference to juniors and seniors, he felt that since juniors have often already made decisions about their future careers, it would be advisable to also include freshman and sophomores. He said he had suggested that to Dr. Humble. Dr. Humble had told him that the NIGMS experience was that their dropout rate was significantly greater for freshman and sophomores. Ms. Haugen noted that freshman and sophomores are still trying to determine what they will do in the future. Dr. Manatou's other suggestion was to use social media to track the students. He said he enthusiastically supports the program, and would like to see funding for more than six of the programs.

Dr. Schantz was the second Council reviewer. She said she was also “incredibly enthusiastic” about the program. She asked Ms. Haugen if there were any statistics about the first cohort of students who had been through the program. Ms. Haugen said she did not have that information at hand but that hopefully the CareerTrac software would help provide those answers. Dr. Schantz asked about the diversity of the faculty mentoring the students. Ms. Haugen said she did not know, but would pass the inquiry along to Dr. Humble.

Dr. Tanguay recommended that the program look into partnering with certain institutions to reach the underrepresented community.

Dr. Brown said he had been very involved with the program at Northeastern. He said the students were invited to be part of their T32 training sessions along with Superfund trainees. He noted that it has become a very popular program that is inundated with applications. He recommended renewal and expansion of the program.

Dr. Cordero said the program was particularly important for first-year students.

Dr. Collman asked for a motion and second to approve the concept, which she received. The Council voted to approve renewal of the program.

VIII. A Strategic Landscape for NIEHS Informatics and Information Technology

NIEHS Deputy Director Rick Woychik, PhD, introduced Dr. David Fargo, Acting Director of Environmental Science Cyberinfrastructure. He presented information on NIEHS informatics and information technology (I&IT), in terms of organization, milestones and strategy, and opportunities and challenges.

He noted that to advance strategic goals in environmental health science and biomedical research, NIEHS requires an agile, robust, and modern cyberinfrastructure. If cyberinfrastructure is to be on the frontlines of innovation and operational excellence, it must extend beyond a traditional information technology (IT) model. NIEHS has created a new Office of Environmental Science Cyberinfrastructure (OESC) to embrace a new model that supports the rapidly advancing scientific and technological landscape. The OESC leads and organizes domain experts with diverse skills, including enterprise IT, scientific IT, data and knowledge management sciences, communications management, bio- and biomedical informatics, computer science, and IT project and program management. The OESC has laid the groundwork for a cyberinfrastructure that fosters a holistic vision for all I&IT at NIEHS.

Dr. Fargo highlighted challenges related to edge computing as well as the implementation of FAIR+ solutions: Findable, Accessible, Interoperable, Reusable, and

Computable), to provide best practice solutions in data and metadata management to the NIEHS community.

Dr. Birnbaum thanked Dr. Fargo for his presentation, which she said made a complicated subject straightforward.

Dr. Ahsan asked Dr. Fargo what type of feedback he was seeking from the Council. Dr. Fargo replied that he would like the Council members' recommendations for how things are working where they are, if there are best practices that NIEHS should be incorporating, if they think NIEHS should be more formally collaborating with the extramural community, and any other suggestions along those lines. Dr. Ahsan noted the emphasis on data sharing in the presentation. He noted that institutions sometimes made such sharing difficult. He said that research participants are often actually quite open to having their data shared. Dr. Fargo said that the larger goal would be to make the data useful and available as soon as possible under policy and governance. He felt that the paradigm for an authentication model should be changed to decrease or eliminate access barriers.

Dr. Manautou asked about protection of intellectual property and reporting of foreign relationships. He asked if there were any guidelines on how to protect information that should not be shared. Dr. Fargo said the balance between sharing and protection is significantly on the side of protection, currently.

Dr. Ho said there is a fundamental conflict between open and closed systems. She noted that security is as vulnerable as the lowest entry point to the system, such as a cell phone. With NIEHS being away from Washington, DC, she asked how it convinces other partners of its security, and how often it is audited. Dr. Birnbaum said that NIEHS is audited frequently. Dr. Fargo said that Dr. Ho's point about the lowest entry point is the driver for substantial upgrades to the NIEHS cyberinfrastructure. It is being built to anticipate needs for firmware updates to instruments, for example. As the science and technology change, the cyberinfrastructure will also change, he observed. He said there is a need to get to a model of much more data-driven access control. He discussed the direction of cloud vendors.

IX. Report of the Director, DERT

DERT Director Dr. Gwen Collman updated the Council on recent developments in the division.

She welcomed new DERT employees Leslie Lynch and Tocarra Chamberlain, and bid adieu to departing DERT official Molly Puente.

She briefed the Council on the 2016-2018 Triennial Advisory Council Report Certifying Compliance with the NIH Policy on Inclusion Guidelines. The report is now due every three years, instead of biennially as was previously the case. It includes data on minority and gender inclusion in NIEHS clinical research projects. The reporting requirements changes slightly under the 21st Century Cures Act. The data are reported as combined extramural and intramural.

Dr. Birnbaum took note of the trend of people not wishing to disclose their ethnicity or gender, and said care must be taken about the issue. Dr. Parker said that it was being seen more and more in graduate school applications. Dr. Collman said that the Council's concern would be communicated to the NIH. She asked for a motion to accept the report, which she received. Council voted electronically in favor of the motion.

Dr. Collman went over Council Operating Procedures and the Council-delegated Authorities for FY2019. She described the roles and responsibilities, procedures, and actions to be addressed by Council. Upon review of other ICs' activities, it was discovered that NIEHS differed in two areas. First, training grants and fellowships do not need to go to Council for second-level concurrence (which had always been done at NIEHS). That will allow awards to move along in a more timely manner, particularly when budgets are delayed. Second, it was discovered that supplements do not need Council action. Dr. Sung commented that he felt there was sufficient knowledge and expertise in the staff to make the decisions about supplements. The Council moved and voted to approve the Council-delegated staff actions for 2019.

Dr. Collman provided a wrap-up of the DERT budget activities for FY2018, which included 1, 431 applications in all categories, 284 competing awards made (191 RPGs, 26 SBIR/STTRs, 24 training grants, 4 centers), with an average cost of a competing RPG at \$373,000 and \$436,000 for non-competing grants. The payline was at the 10th percentile for R01, R03, and R21 grants, and the NIEHS success rate was 17.1% for all RPGs and 16.6% for R01s. She related data on the various breakdowns of the RPGs. She also discussed the 2018 Superfund funding, and listed NIEHS co-funded initiatives with other ICs in FY2018. She also described DERT's current practices for funding decisions.

Dr. Sung asked what the basic requirements are to be eligible for consideration to be an "At Risk" investigator. Dr. Collman said that most of the "raise-to-pays" (applications outside the announced payline but that are considered for funding) fall in the 10th percentile to 25-30, but that program staff look further than percentile. Dr. Sung asked how long a grant remains eligible for raise-to-pay consideration. Dr. Collman replied that a grant remains eligible all year. She added that if an investigator is on a raise to pay list and is not picked up at the beginning of the year, the application should be revised and resubmitted.

Dr. Wright wondered if NIA might be a good partner for Alzheimer's-related initiatives. Dr. Collman said that had been considered and may be possible in the future

X. Ensuring Future Impact: Strategic Realignment in the DNTP

Dr. Brian Berridge, DNTP Scientific Director and NTP Associate Director, gave his first presentation to the Council in those roles. He provided a short biography, including information about his specialties and scientific interests. He described the mission and goals of the NTP in the context of what attracted him to join the organization. He said that what drew him the most was the aspiration to evolve toxicology from an observational science to a predictive one that was articulated as a 21st century vision for NTP and has been embraced by the field. With NTP in an exciting place, there remain significant needs to fulfill the envisioned transition:

- To address a rapidly increasing portfolio of concerns
- To respond to a broad stakeholder group with changing expectations
- To bring more human relevance and individual precision to our hazard characterizations
- To build confidence in a different approach to assessing hazards
- To decrease our dependence on animals as a primary modeling platform

NTP also faces a variety of opportunities:

- An aspiration
- Advances in technology
- Willingness to innovate and take risks
- An ability to leverage our experiences
- Really smart and dedicated staff and partners

Dr. Berridge described several messages that have emerged from his engagement with the NTP Board of Scientific Counselors. He said that there has been progress in the application of the breadth of NTP capabilities, which may have been applied *ad hoc* and in isolation in the past, but recently there has been a deliberate effort to integrate the various assessments to support novel approaches. He presented the DNTP Translational Toxicology Pipeline concept, which is designed to leverage a number of key opportunities to allow the field to become more predictive, particularly of human health effects. Evolving the NTP portfolio content will allow improved sustainability and impact. He noted the intent to concentrate on health effect innovation in three key areas of public health:

- Carcinogenicity Testing for the 21st Century
- Developmental Neurotoxicity Modeling

- Cardiovascular Hazard Assessment in Environmental Toxicology

In summary, Dr. Berridge noted:

- DNTP and the NTP are at a clear intersection of need and opportunity.
- A history of impactful science, a portfolio of capabilities, and an expert staff optimally position us to innovate the way we do toxicology.
- Iterative learning is key to delivering on our aspiration.
- We'll embrace fundamental scientific challenges to advance the field.
- An effective communication strategy for all stakeholders will be necessary to optimize the impact of our science.

Dr. Mendrick asked Dr. Berridge to share his thoughts about translation and extrapolation of rodent results to humans. Dr. Berridge replied that the role of animal studies is a topic of much debate, as is extrapolation from even the complex 3D systems to an *in vivo* outcome. He noted that purists still resist that, because it skips the animal stage. He said that although he is an advocate to decrease dependence on animals, the current reality is that animal studies are still a critical part of the portfolio.

Dr. Cordero asked where the issue of mixtures would fit in the new paradigm. Dr. Berridge said NTP would continue to do agent-based investigations, but taking on other investigations would create more balance in how NTP does its business. Addressing mixtures would take the full spectrum of NTP's capabilities, he observed. He said that all of the available tools would be needed in a structured and strategic way to start to chip away at the challenge of mixtures.

Dr. Ahsan asked how some of the ideas Dr. Berridge had presented would be integrated into NIEHS as a whole. Dr. Birnbaum noted that there is One NIEHS, with interaction and cross-fostering going on regarding those ideas. Dr. Berridge said that there are increasing opportunities to bridge between divisions, and that partnerships are critical.

Dr. Manautou said he was intrigued by Dr. Berridge's concept of pathobiology as a continuum, with maladaptive physiology as a precursor to full-blown pathological observations. He said he was interested to hear more about the concept, how to address it experimentally, and how to incorporate it into the process of defining pathological outcomes. Dr. Berridge said that he likes the (Adverse Outcome Pathway) AOP concept, because it allows you to start identifying the critical transition points.

Dr. Shih highlighted the risk communication area. He said that more activity would engage the community more, and would leverage the knowledge generated by NIEHS to affect policy. Dr. Birnbaum noted that NTP has an extremely active risk communication effort, including by using social media, that has been increased over the

last year or two to ensure that all stakeholders are adequately informed. Dr. Berridge said that engaging stakeholder groups is critical for NTP.

Dr. Ahsan mentioned the importance of toxicological assessment of multiple agents.

XI. Summary of the NIEHS SBIR/STTR Program

Dr. Dan Shaughnessy provided the Council with an overview of the NIEHS SBIR/STTR program and updates on its activities.

The Small Business Innovation Research (SBIR) Program is a set-aside program for small business concerns to engage in federal research and development, with potential for commercialization. It requires agencies with an extramural budget of \$100 million or more to set aside 3.2% of those funds to the SBIR Program. The Small Business Technology Transfer (STTR) Program is a set-aside program to facilitate cooperative R&D between small business concerns and U.S. research institutions, with potential for commercialization. It requires agencies with more the \$1 billion in funding to participate in STTR, a .45% set-aside.

NIEHS programs concentrate in the following areas:

- Exposure assessment tools
- Nano environmental health/safety
- Toxicity screening, testing, and modeling
- Biomarkers
- Education and outreach
- Superfund Research Program (a separate SBIR set-aside)

Dr. Shaughnessy provided details about the various programs funded by NIEHS SBIR/STTR, including current solicitations:

- RFA-ES-17-008: Organotypic Culture Models Developed from Experimental Animals for Chemical Toxicity Screening (R43/R44)
- RFA-ES-18-008: Novel Approaches for Characterizing Exposure and Response to Engineered Nanoparticles (R43)
- RFA-ES-19-005: Innovative Approaches for Improving Environmental Health Literacy (R43/R44)
- RFA-ES-19-006: Innovative Approaches for Improving Environmental Health Literacy (R41/R42)

He described each of the RFAs and mentioned several of the grant recipients as examples.

He discussed current efforts to improve commercialization and return on investment, particularly efforts to help companies to bridge the so-called “valley of death.” NIH has programs to assist commercialization at each stage of the process.

He cited the various methods that have been developed to allow the program to track the progress and success of its grantees.

Dr. Wright asked about the program’s involvement with wearable devices and the Internet of things. Dr. Shaughnessy said that the program has invested much in those areas, particularly in air pollution sensors. He noted that price point is an ongoing issue. Dr. Wright asked about monitors that link to GPS. Dr. Shaughnessy said that development of that type of technology has been supported in the past, and remains a topic of interest.

Dr. Rob Tanguay asked how to change the culture for R01 investigators to think that commercialization is actually a good thing. He noted that in his own institution, he has met with resistance from traditional views of commercialization. He felt that more effort to change the culture is needed. Dr. Shaughnessy agreed, and noted that as a set-aside program, all of the NIH institutes have a substantial amount of funding to devote to the effort. He acknowledged that investigators sometimes end up spending a substantial amount of their time working on the business aspects of commercialization, and so the programs for assistance are increasing important. Dr. Birnbaum said that rather than resistance, she is hearing more often that academics are busy starting their own companies. Dr. Rob Tanguay replied that the phenomenon he was describing seemed to concentrate in certain disciplines, where there is rigid opposition, almost on moral grounds. Dr. Collman noted that some universities have invested in incubator strategies, with support staff to help entrepreneurial academics. Dr. Shaughnessy described the REACH program, and institutes that have developed innovation zones to encourage people with good ideas and promising technologies. Dr. Birnbaum observed that NIH is required to spend 3.2% of its budget on SBIR, and an additional smaller percentage (0.45%) on STTR, which adds up to a substantial amount of money. Dr. Collman noted that the requirements apply to every federal agency.

XII. Adjournment

Dr. Birnbaum thanked everyone who had contributed to a very successful meeting.

The meeting was adjourned at 10:38 a.m., February 21, 2019.

CERTIFICATION:

/s/

Linda S. Birnbaum, PhD, DABT, ATS
Chairperson
National Advisory Environmental
Health Sciences Council

Attachment:
Council Roster

/s/

Gwen W. Collman, PhD
Executive Secretary
National Advisory Environmental
Health Sciences Council