

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

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

June 6-7, 2017

The National Advisory Environmental Health Sciences Council convened the open session of its one hundred fifty-first regular meeting on June 6, 2017 in the Rall Building, Rodbell Auditorium, National Institute of Environmental Health Sciences, Research Triangle Park, NC. The closed session of the meeting was held earlier the same day.

The meeting was open to the public on June 6, 2017 from 10:30 a.m. to 5:00 p.m. and on June 7, 2017 from 9:00 a.m. to 11:00 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 June 6, 2017 from 8:30 a.m. to 10:15 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)
Jeanne Conry, MD, PhD
Irasema Coronado, PhD
Kevin Elliot, PhD
Brenda Eskenazi, PhD (via WebEx)
Kenneth Fasman, PhD (via WebEx)
Andrew Feinberg, MD (June 6)
James Johnson, Jr., PhD (*ex officio*)
Maureen Lichtveld, MD (via WebEx)
José Manautou, PhD
Marie Lynn Miranda, PhD
Donna Mendrick, PhD (*ex officio*)
Deborah Winn, PhD (*ex officio*)
Lauren Zeise, PhD (via WebEx)

NIEHS Staff

Janice Allen, PhD
Trevor Archer, PhD
John Balbus, MD
David Balshaw, PhD
Martha Barnes
Linda Bass, PhD
Bryann Benton
Linda Birnbaum, PhD
Tiffany Bowen
John Bucher, PhD
Jed Bullock
Danielle Carlin, PhD
Trisha Castranio
Lisa Chadwick, PhD
Kelly Chandler, PhD
Pam Clark
Gwen Collman, PhD
Yuxia Cui, PhD
Sally Darney, PhD
Christie Drew, PhD
Chris Duncan, PhD
Lisa Edwards
Symma Finn, PhD
Christine Flowers
Amanda Garton
Barbara Gittleman
Virginia Guidry, PhD
Janet Hall, MD
Astrid Haugen
Michelle Heacock, PhD
Heather Henry, PhD
Jon Hollander, PhD
Guang Hu, PhD
Chip Hughes
Michael Humble, PhD
Bonnie Joubert, PhD
Helena Kennedy
Alfonso Latoni, PhD
Cindy Lawler, PhD
Kelly Lenox
Chris Long
Sarah Luginbuhl
Ron Mason, PhD
J. Patrick Mastin, PhD
Kim McAllister, PhD
Steven McCaw

Rose Anne McGee
Liz McNair
Sri Nadadur, PhD
Sheila Newton, PhD
Aaron Nicholas
Liam O'Fallon
Suzy Osborne
Nicole Popovich
Molly Puente
Lingamanaidu Ravichandran
Scott Redman
Jim Remington
Elizabeth Ruben
Maria Shatz, PhD
Thad Schug, PhD
Dan Shaughnessy, PhD
Ashley Singh
William A. Suk, PhD, MPH
Kimberly Thigpen Tart, JD
Ian Thomas
Laura Thomas, PhD
Claudia Thompson, PhD
Brittany Trottier
George Tucker
Steven Tuyishime, PhD
Fred Tyson, PhD
Michelle Victalino
Leroy Worth, PhD
Rick Woychik, PhD
Demia Wright
Darryl Zeldin, MD

NIH Staff

Meena Ananthanarayanan, PhD, NIH/CSR (by phone)
Lawrence Tabak, DDS, PhD, NIH (via WebEx)
Tasmeen Weik, DrPH, MPH, NIH/CSR (by phone)taba

Members of the Public Present

Maureen Avakian, MDB, Inc.
Christie Barker-Cummings, SSS
Michael Easterling, SSS
Ernie Hood, Bridport Services, LLC
Kerry James, SSS
Richard Rosselli, SSS

Donna Spiegelman, PhD, Harvard University

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. Eskenazi and *ex officio* Council Members Drs. Hann and Cibulas were unable to attend. She said that Drs. Brown, Eskenazi, Fasman, Lichtveld, and Zeise would be attending via WebEx. She asked all present in the room to introduce themselves, which they did. She asked the Council members attending via WebEx 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.

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 February 2017 Meeting Minutes

Approval of the February 2017 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 updated Council on Institute developments since the February 2017 Council meeting.

She began with a report regarding appropriations. For Fiscal Year 2017, the NIEHS budget increased by \$20.7 million. The President's Request for FY2018 totals \$593.144 million, which is \$198.466 million or 25.07 percent less than the total amount appropriated for NIEHS in FY2017. Dr. Birnbaum expressed confidence that members of Congress would be unlikely to support such large cuts, but the situation going forward remains uncertain.

She described several new pieces of proposed legislation that potentially affect NIEHS, including the Airplane Impacts Mitigation Act of 2017, the Federal Accountability in

Chemical Testing Act, the Investing in Testing Act of 2017, an act mandating education and training for environmental health professionals, the Radiation Exposure Compensation Act Amendments of 2017, and the Feminine Hygiene Product Safety Act of 2017. She expressed doubt that any of the proposed laws she had described would go forward.

Turning to science advances, Dr. Birnbaum briefly summarized several recent publications by NIEHS/NTP personnel or grantees. First, as an example of “One NIEHS” research, she described a publication called “Associations Among Personal Care Product Use Patterns and Exogenous Hormone Use in the NIEHS Sister Study.” She also provided short summaries of recently published studies from DIR, DNTP, and DERT researchers.

In NIEHS news and highlights, she described new outreach and engagement initiatives involving science literacy, a health disparities curriculum, a tribal consultation, a new newsletter from the Superfund Research Program, a plenary talk by NIEHS Deputy Director Dr. Rick Woychik at the 2017 State of the Gulf of Mexico Summit, and an ICCVAM Public Forum held in May. She provided details about NIEHS interagency activities related to per- and polyfluoroalkyl substances (PFAS) involving 17 federal agencies, and NIEHS involvement in the WHO IPCS Systematic Review.

Dr. Birnbaum noted NIEHS participation in the Molecular Microscopy Consortium, a joint venture with Duke University and the University of North Carolina at Chapel Hill, which has acquired a powerful Cryo-EM electron microscope for research use by consortium members.

She described several noteworthy recent meetings and events, including a toxic metals symposium, a workshop on Environmental Risks for Psychiatric Disorders, a Superfund Worker Training Grantee Meeting and Community Forum, and a symposium and workshop devoted to Epigenetics, Stem Cells, and Environmental Health.

She recognized awards recently given to NIEHS personnel and grantees from the Endocrine Society, the Society of Toxicology, the HHS Green Champions program, the Cure JM Foundation, the American Board of Toxicology, the American Society for Clinical Investigation, the Champion Awards, and the Goldman Environmental Prize. She recognized the latest group of NIEHS ONES grantees.

Dr. Spiegelman asked whether NIEHS might be considering partnerships with the military, given the potential direction of the federal budget. Dr. Birnbaum said it was a great suggestion, and that the institute has already begun some discussions with military and Department of Defense officials. She discussed several other new aspects of federal funding of NIEHS research, such as possible overhead reductions.

Dr. Manautou asked what percentage of NIEHS grantees are located outside of the United States. Dr. Birnbaum said that in terms of principal investigators, the number is very small. She noted that as of 2015, NIEHS funded just over 100 studies with work being conducted outside the U.S.

Dr. Miranda asked Dr. Birnbaum for her impression of how well Congress people understand what indirect costs are. Dr. Birnbaum noted that with research being funded in every district, many universities are extremely active in educating representatives about overhead.

Noting the potential closure of the Fogarty Center, Dr. Feinberg asked about the possibility of NIEHS partnering with international entities where research funding is actually being increased. Dr. Birnbaum noted that NIEHS cannot directly get funding over and above what Congress appropriates, although partnerships can and have been developed in a number of areas. Dr. Collman mentioned that there have been international partnerships developed through the Fogarty Center where the funding is kept separated, with the overseas portions funded by the countries involved, and that that could be a model for future programs. Dr. Birnbaum noted that the total budget for the Fogarty Center is less than \$70 million.

V. The NIH Director's Pioneer Award Meets Biostatistics: Next up, the meeting of environmental health and implementation science?

In August 2017, longtime NIEHS grantee Dr. Donna Spiegelman from Harvard University will start the fourth year of her five-year NIH Director's Pioneer Award. The goals of the award concern the development and promulgation of advanced methods to facilitate implementation science and large-scale public health evaluations, thereby achieving the trademark Pioneer "high risk/high reward" objective. She is re-orienting her career focus from etiologic research and statistical methods arising from such work, especially as they had concerned methods to adjust for bias due to exposure measurement error. She provided an overview of basic concepts in implementation science and the overlap of methods used with methods constituting the traditional epidemiologic and biostatistical tools. She also summarized the accomplishments thus far in her Pioneer Award program, and described plans for the next two years. She said she was particularly interested in stimulating discussion aimed at strengthening the implementation science approach to large-scale public health evaluations in environmental health.

Dr. Conry asked Dr. Spiegelman about guidance on implementation strategy related to well woman guidelines under the Affordable Care Act. Dr. Spiegelman replied that she had a study design that may be useful in that effort. She noted that data sharing can be a challenge in that type of research.

Dr. Ahsan asked about the role of social sciences such as economics in biomedical research. Dr. Spiegelman said that the ideal research team should include biostatisticians, epidemiologists, social scientists, and modelers.

VI. Strategic Plan Updates

A. Overview: Dr. Linda Birnbaum, NIEHS and NTP Director

The next session of the meeting was designed to update Council members on the status of the current 2012-2017 NIEHS Strategic Plan, with members of Institute leadership reporting on their sectors' implementations, and to begin the process of arriving at a new strategic plan to begin in 2018.

Dr. Birnbaum introduced the session. She summarized the process that guided the effort to draft the 2012-2017 strategic plan, *Advancing Science, Improving Health: A Plan for Environmental Health Research*. She recounted the eleven Strategic Goals in the existing plan, which have guided the Institute's research priorities and decision making across its divisions over the past five years. She also described the nine One NIEHS goal-related priority areas that were identified by multiple divisions as part of the plan's implementation process.

She emphasized that the current plan has been a living, breathing document, with each division following its elements to guide its work over the past five years.

Strategic Goal #1: Identify and understand shared mechanisms or common biological pathways.

Strategic Goal #2: Understand individual susceptibility across the life span to chronic, complex diseases resulting from environmental factors.

Strategic Goal #3: Transform exposure science.

Strategic Goal #4: Understand how combined environmental exposures affect disease pathogenesis.

Strategic Goal #5: Identify and respond to emerging environmental threats.

Strategic Goal #6: Establish an environmental health disparities research agenda.

Strategic Goal #7: Use knowledge management techniques to create a collaborative environment for the EHS community and encourage an interdisciplinary approach.

Strategic Goal #8: Enhance the teaching of EHS at all levels to increase scientific literacy and generate awareness of the health consequences of environmental exposures.

Strategic Goal #9: Train the next generation of EHS leaders.

Strategic Goal #10: Evaluate the economic impact of policies, practices, and behaviors that reduce exposure to environmental toxicants.

Strategic Goal #11: Promote bidirectional communication and collaboration between researchers and stakeholders.

B. Office of the Director (OD): Dr. Birnbaum

Dr. Birnbaum provided the initial division-specific summary of implementation activities and accomplishments related to the 2012-2017 Strategic Plan goals.

She reiterated the One NIEHS concept, and noted that much of what the OD does crosses multiple Strategic Plan goals. In addition to the OD (the Director and Deputy Director) providing leadership for the Institute as a whole, the various offices under OD (the Office of the Deputy Director (ODD), the Office of the Director, Bethesda (ODB), the Office of Planning, Policy, and Evaluation (OPPE), the Office of Communications and Public Liaison (OCPL), and the Office of Science Education and Diversity (OSD)) were responsible for their own implementation activities and accomplishments, which Dr. Birnbaum highlighted.

She focused on activities and accomplishments related to Strategic Goals 5, 6, 7, 8, 9, and 11.

C. Division of the National Toxicology Program (DNTP): Associate Director Dr. John Bucher

Dr. Bucher summarized DNTP highlights responsive to the 2012-2017 Strategic Plan. "Many of the programs that NTP does are multi-year programs, and some build on things that have been going on beforehand and will continue to go on well after 2017," he told the panel. He described DNTP activities and accomplishments related to Strategic Goals 1, 2, 3, 4, 5, 7, 9, 10, and 11.

Dr. Feinberg commented, "This is a healthy, vigorous, evolving execution of some really great ideas, and particularly in a time of money discontinuity, it seems really important to have some sustained vision that carries forward." He suggested that it may be worth considering extending the life of a strategic plan to 7 or even 11 years. He asked Dr. Birnbaum for her thoughts on that concept. She replied that "five years is a reasonable number for looking at where you've been and where you're going." She noted that large changes are not anticipated, but with the formulation of a new plan there are opportunities to tweak, to add, or to change focus.

D. Office of Management (OM): Associate Director for Management Chris Long

Mr. Long described the organization and resources of the Office of Management for the panel members, which exists “for the sole purpose of helping the science happen.”

The OM Implementation Plan included the intent to support and enable all of the Strategic Plan goals, with a special focus on Goals 5, 7, 8, and 9.

He stressed the importance of agility and continuity in the OM’s work, because “we have to be able to flex,” in important areas such as acquisitions, budget and operations, and security.

E. Division of Intramural Research (DIR): Scientific Director Dr. Darryl Zeldin

Dr. Zeldin described the workings and organization of DIR, where research is investigator-initiated and peer-reviewed by the Board of Scientific Counselors (BSC). Principal investigators are required to discuss how their work relates to the Strategic Plan in their presentations and reports to the BSC. Strategic Plan relevance is one of the criteria used by the BSC in principal investigator evaluation. DIR was reorganized in 2014, with one purpose being to move in new scientific directions in support of the Strategic Plan. That resulted in sunseting of programs and research groups not well-aligned with the plan.

Dr. Zeldin mentioned the division’s new hires since 2012, including 14 Principal Investigator-level scientists, and related each to the Strategic Plan goals to which their work relates. He detailed DIR’s activities related to Goal #9, noting that training is a major focus of DIR efforts, with approximately 180 trainees currently in the division.

He outlined several other activities within DIR that align with Strategic Plan goals, including ongoing large environmental cohorts (Goals 1, 2, 3, & 4), the Environmental Polymorphism Registry (Goals 1, 3, & 4), the Disaster Research Response Program (Goal 5), Cross Divisional Working Groups (Goal 1), Global Environmental Health Sciences (Theme 4), and research conducted by DIR, which has been quite prolific within the five-year plan period.

Dr. Manautou asked Dr. Zeldin to elaborate on the 30% reduction in the number of trainees he had mentioned. Dr. Zeldin replied that the reduction was entirely budget driven. He noted that the number of principal investigators and lab size had also been reduced over the past several years, resulting in fewer opportunities for trainees. Dr. Manautou asked if Dr. Zeldin had seen a trend in the number of applications for training slots. Dr. Zeldin said that many of the postdoctoral positions are not filled through the application process, but he speculated that most of the Principal Investigators (PIs)

probably receive from 5-10 emails per day from people interested in NIEHS postdoc positions.

Dr. Elliott asked about how the work of the DIR core centers might connect with the Strategic Plan's provisions for engagement and communication. Dr. Zeldin said that within capacity limitations, the core centers, including the Clinical Research Unit, welcome outside researchers to use the resources. Dr. Elliott asked about DIR interaction with community groups. Dr. Zeldin replied that DIR does not typically meet with community groups, given that the division is not as "community out-facing" as DERT or OD. Dr. Birnbaum added that DIR epidemiologists are community out-facing and meet with community groups as part of their work.

Dr. Mason, the PI of the Free Radical Biology Group, acknowledged the reduction in the number of trainees, but said that the remaining trainees are high quality. "We can recruit good people here, but not as many as I would like," he commented.

F. The Clinical Research Branch (CRB): Clinical Director Dr. Janet Hall

Dr. Hall related the work of the Clinical Research Branch to the six overall themes described in the Strategic Plan. She described the activities and organization of the branch. Citing several specific examples, she aligned CRB research with Strategic Plan Goals 1, 2, 3, 4, 5, 6, 8, and 9.

Dr. Coronado asked about the status of the Environmental Polymorphism Registry. Dr. Hall said the majority of the patients were collected through specific drives early in the program, and that recruitment through anyone coming into the Clinical Research Program continues.

Dr. Manautou asked if there had been any analysis of the Registry samples so far. Dr. Hall replied that the program is intended to be a biobank repository, and was not set up as an epidemiologic study, although some important scientific questions can be asked going forward. Analysis thus far has primarily focused on looking at specific genes.

G. Division of Extramural Research and Training (DERT): Director Dr. Gwen Collman

Dr. Collman reviewed the division's many accomplishments in implementing the 2012-2017 Strategic Plan. Implementation of the plan has been a division-wide effort involving implementation teams for each of the plan's goals (except Goal 8). She concentrated her summary on the key measures of success, including Funding Opportunity Announcements (FOAs), publications, collaborations, resources, and meetings. With grants being so complex and often addressing more than one Strategic Plan goal, Dr. Collman presented charts visually depicting the primary goals for newly

awarded projects and subprojects from 2011-2016. The chart illustrated growth in certain areas over the course of the Strategic Plan, such as emerging threats and health disparities.

She also showed the results of a survey of the goal implementation teams, who were asked to describe what they considered to be the top three accomplishments in their areas.

DERT Strategic Plan Goal outputs included:

- 25 resources/tools
- 126 webinars, workshops, special sessions, and symposia
- 54 collaborations (with entities outside NIEHS)
- 52 FOAs to promote research in Strategic Plan goal areas
- 63 highlighted publications, with 30 from NIEHS-supported workshops
- 35 podcasts

Dr. Collman shared a variety of stories exemplifying activities related to specific goals.

Dr. Coronado asked Dr. Collman about the availability of the MicroPEM, a device designed to measure personal particulate matter exposure. Dr. Collman said she would supply Dr. Coronado with contacts at RTI, the vendor for the device.

Dr. Miranda said she had enjoyed Dr. Collman's phrase about "wearing the Strategic Plan every day." In the areas of sensor and technology development and methods development, she suggested emulating Silicon Valley companies, which regularly get people to work on problems for free through Grand Challenges. Dr. Birnbaum noted that NIEHS has conducted several of those types of competitions, and has encouraged development through SBIR/STTR activities.

H. Renewing the NIEHS Strategic Plan: Dr. Sheila Newton, Director, Office of Policy, Planning and Evaluation

Dr. Newton briefed the Council on plans for the next iteration of the NIEHS Strategic Plan, which will run from 2018-2023. She said that the previous speakers had shown clearly that the current Strategic Plan had truly functioned as a roadmap for decisions and priorities over the past five years.

Looking at the next planning process, she described assumptions to base planning upon:

- The 2012-2017 Strategic Plan has been a useful framework for helping our decision making regarding research priorities and opportunities.

- Some parts of the Plan will continue to be relevant to current scientific realities, needing just some updating.
- Other parts of the Plan deal with areas that have changed dramatically since 2011.
- It will not be necessary to start from scratch like we did in 2011.
- Bottom Line: We will use the existing Plan as a starting point for developing a new 5-year strategy for 2018-2023.

The first step in the process will be to ask for input from the community, via an online survey titled *Trends & Insights: Next Steps for NIEHS*. The survey will be available online through August, 2017. In September, 2017, there will be Council discussion of new ideas and input for the Strategic Plan, as well as presentation of preliminary results from online input. In late October, 2017, full analysis of Council discussion and online input will take place, to be followed in November and December by drafting of new goals and subgoals, with an initial draft of the new plan posted to the Web in early January, 2018. In February, the initial draft will be presented and discussed at Council. From April to June, 2018, the new plan text will be finalized. July to September will see editing, addition of images and layout work. The final plan will be presented to Council in September, 2018, with publication anticipated in October, 2018.

Dr. Coronado asked whether there was a way for non-English speakers to participate, or people lacking internet access. Dr. Newton said that written comments submitted would be welcome, with arrangements for translation.

Dr. Zeise said that while reflecting on priorities and trends in the field, it was useful to consider the downstream impacts. She wondered if any measures of impacts of the research had been gathered, and if so such a discussion would be accessible on the internet. Dr. Newton noted that the Goal 10 implementation group within DERT had worked on that area. Dr. Christie Drew noted the availability of a new resource devoted to economic evaluation of environmental health, with an annotated bibliography. More broadly, there is a program called HITS, the High Impact Tracking System. Dr. Collman added that this is an internal tool, but there has not been an institute-wide effort to evaluate impact through a systematic approach. Dr. Zeise said that the institute's portfolio is so mind-boggling that it is difficult to sort through it and weigh priorities. Dr. Newton said she concurred with that conclusion, and that past efforts have been concentrated in specific areas. She added that to evaluate impact on a wider basis would be extremely work-intensive.

Dr. Fasman praised the work NIEHS had done in the past several years in the strategic planning area as "exemplary." He said, "I've been involved in a lot of strategic planning exercises in a lot of scientific organizations, and I have never seen an exercise that has been started and carried all the way through so well, including your very thoughtful and

sensible plan for this next phase.” He suggested that NIEHS prepare a publication about the entire process, so that it could serve as a model for other organizations.

Dr. Feinberg agreed, noting that there are lessons from the process that could be generalized across NIH as a whole.

Dr. Litchveld particularly complimented the work that has been done in the extramural area. She offered her assistance in an area called enterprise evaluation. She asked whether the new plan would be taken on the road nationwide for in-person, community stakeholder feedback. Dr. Birnbaum replied that although that was an interesting idea, the need was not evident at this time. Dr. Newton note that there were a couple of opportunities she had not included in her timeline, such as regularly occurring in-person meetings with stakeholder groups.

VII. Embryonic Stem Cells: From Developmental Biology to Environmental Health Sciences

Dr. Trevor Archer, chief of the NIEHS Epigenetics and Stem Cell Laboratory, introduced Dr. Guang Hu, who briefed the Council on his lab’s work.

He provided background scientific information about pluripotent stem cells, which he said hold great promise for both basic and translational research. He said that the long-term goal of his research is to better understand the molecular mechanisms that regulate embryonic stem cell (ESC) self-renewal and differentiation. His group previously carried out a genome-wide RNAi screen in mouse ESCs and identified a list of novel regulators of ESC self-renewal. They have since investigated the function of several of the identified factors in ESCs, somatic cell reprogramming, and mouse embryonic development. They have also uncovered novel mechanisms such as mRNA deadenylation, mRNA export, mRNA alternative polyadenylation, and chromatin remodeling in the regulation of the ESC state. In the future, Dr. Hu and his team will continue to investigate ESC self-renewal and differentiation using genetic and genomic approaches. They are also collaborating with other labs to use ESCs to explore environmental health science questions. Specifically, they will initially use human ESC differentiation as a culture model to investigate the developmental toxicity of selected environmental compounds. Eventually, reporter cell lines and screening conditions will be established to systematically dissect the roles of environmental factors in development and diseases. The research could provide new insights into mammalian development and facilitate the use of pluripotent stem cells for translational and environmental health research.

Dr. Mendrick asked whether Dr. Hu had considered looking at impeding differentiation in ESCs. He replied that the system he employs is set to both promote and impede

differentiation. He said that from a basic research perspective, it is more interesting to identify ways to increase differentiation specificity and efficiency.

Dr. Manautou asked whether there was any effect on cell number or viability at the early stage of development, when cells are exposed to TCDD. Dr. Hu said that no changes in cell number, cell cycle distribution, or apoptosis were seen during that window. Dr. Manautou asked whether changes in half-life were also seen in other pluripotency genes beyond Cnot3. Dr. Hu said none exhibited changes in half-life

Dr. Birnbaum asked Dr. Hu what concentration of TCDD he had used. He said he had used 1 nanomolar, where a consistent and reproducible effect was seen.

VIII. Enhancing Stewardship: The Next Generation of Researchers Initiative

Dr. Lawrence Tabak, Principal Deputy Director, NIH, briefed the Council on the new NIH initiative designed to address the currently imbalanced situation in the age of the biomedical workforce. The current hypercompetitive funding environment, which skews to the benefit of older investigators, is discouraging younger, less established researchers who may find their grant applications are not approved. This creates an aging workforce as struggling early- and mid-career scientists depart the field.

Under the 21st Century Cures Act, NIH has been directed to establish the Next Generation of Researchers Initiative, which focuses on promoting and providing opportunities for new researchers and earlier research independence. One method for doing so will be to extend the payline for early stage investigators. Also, efforts will be made to prioritize support for mid-career investigators who just missed funding for their first competitive renewal, or who are seeking support for their second RPG, by providing new support systems.

Dr. Tabak said that all NIH ICs have committed to ensuring support for highly meritorious early-stage and mid-career investigators. The NIH Office of the Director will create an inventory of early- and mid-stage investigators within the fundable range (currently defined as equal to or better than a percentile of 25% or impact score of 35), and will track IC funding decisions involving those investigators with fundable scores, to evaluate whether uniform decision making is occurring across NIH.

For early-stage investigators who have been a principal investigator for ≤ 10 years and are about to lose all NIH funding, and PIs who are seeking a second award, NIH plans to invest an initial estimated \$210 million, ramping up to a steady state of \$1.1 billion per year after five years. The support will come from reprioritization of funds, with flexibility

among the ICs as to how they will provide it. This will facilitate funding to the 25th percentile.

Dr. Tabak also spoke about the need to assess the impact of NIH research by developing metrics of productivity. He mentioned that NIH has been exploring approaches to create a modified “grant support index.” In the long term, the value of NIH investments may be assessed by measuring outcomes such as”

- Disruptions in prevailing paradigms
- Patents/licenses
- New technologies
- New medical interventions
- Changes to medical practice
- Improvements in public health

Further, there is a need to develop sophisticated methods to measure the interim influence of NIH funding.

Dr. Birnbaum invited discussion and comments from Council members.

Dr. Manautou asked what criteria were used to select the percentile, noting that it would be “quite far away from the payline of some institutes.” Dr. Tabak said that it was not quite far away from the payline of the NIH as a whole. “I think that what we’re looking at with that group of applications is highly meritorious science,” he noted. He mentioned the severe compression of scores at study sections in recent years, resulting in the fact that “we are leaving a great deal of outstanding work unsupported.” Dr. Manautou asked if there are institutes with a much larger proportion of investigators in the age group to be supported, implying that there could be a significant financial burden to such an institute. Dr. Tabak said he had not seen institute-by-institute data, and that there was no intent to “put institutes and centers in harm’s way.” He noted that IC directors will drive the decision making as they decide how and what to reprioritize, and centrally, NIH will be tracking demographics.

Dr. Miranda asked if NIH had thought about investing in a “posse effect,” or economies of scale, with NIH selecting the institutions and the institutions select the individual investigators to be supported, thus encouraging the institutions to put supporting networks in place. She said she had found such arrangements to be extremely powerful. Dr. Tabak said that that approach had been discussed, but the challenge was seen to be that institutions have such different business models, some of which would not be conducive to such an approach, leading to some seeing it as another unfunded mandate from the federal government. Dr. Miranda noted that the AAU had characterized university business models into 3 or 4 bins, and said she was not

convinced that the approach she mentioned could not be made to work with the various business models. Dr. Tabak thanked Dr. Miranda for raising the issue, and said he would take another look at the idea.

Dr. Elliott asked Dr. Tabak to clarify the connection between the second half of his presentation, which dealt with metrics, and the first half, which described early investigator support. Dr. Tabak said the metrics would be developed to help with the reprioritization process described in the first half of the talk. "If we had a validated way of being able to assess our portfolio without having to wait 40 years to see how things turn out," he said, "that would be a good tool that an IC director or their staff could make use of." He said it had been concluded that such an approach did not yet exist.

Dr. Coronado asked what evidence Dr. Tabak has about investigators leaving the workforce, and where they would work. Dr. Tabak replied that clinicians go into practice and are lost to the biomedical research workforce. PhDs also pursue other careers, and in some extreme instances may drop completely out of science. At some institutions, investigators who are not funded are not allowed to stay, he noted. "We are trying to prevent that from happening," he said. "It would be a shame, after investing so much in the training of these individuals, to see them lost to the workforce."

Dr. Ahsan asked whether it had been considered to allow institutes to set their own mechanisms for funding the program. Dr. Tabak noted that IC directors were being given "a tremendous degree of latitude," and they will decide, based on their own priorities, how best to approach the issue. He said that the target of the 25th percentile is for the overall agency.

Dr. Miranda commented about the loss of physician scientists, noting that almost every area of biomedical research has become more quantitative. Medical school curricula, however, are not adjusting to that trend. She suggested that institutions need to do so. She pointed out a gap between the quantitative knowledge of people coming out of medical school and the quantitative knowledge necessary to be successful in grant writing. Dr. Tabak said that Dr. Miranda had raised a crucially important point, which applies to many PhD programs as well as medical schools. He felt that quantitative science needs to be embedded in every graduate program.

Dr. Birnbaum said the Council seemed to be quite pleased with the evolution of the policy. Dr. Tabak thanked the Council for several important suggestions. Dr. Birnbaum noted that the policy had been initially presented to IC directors just one month previously, and the evolution has been dramatic (Dr. Tabak had presented the plan to several other IC Councils in the interim). She said she was pleased to hear about the flexibility being allowed the individual ICs in reprioritizing. She suggested that expansion of the ONES program may be one way for NIEHS to move forward.

Dr. Manautou asked if there was any idea of how many NIEHS grantees or applicants might fall into the category being addressed and the financial burden to the institute. Dr. Collman described the metrics NIEHS uses to track the situation. She added that there would be a closer look at the mid-career investigators' success, and that it was good to hear there would be latitude in how to work on the situation if necessary.

Dr. Miranda asked where allocations may be reduced, with a fixed budget. Dr. Collman said that had not yet been considered. Dr. Miranda noted that there is "no fat in the budget." Dr. Collman said it had always been difficult to identify scientific areas of lesser priority. She acknowledged that this was a different situation, however. Dr. Birnbaum added that full discussion by Council in its September meeting would be helpful. She described the age imbalance situation in more detail, including the fact that NIH buying power has declined since 2003. She noted that many of the older investigators actually provide much of the training in the field, but the metrics have not been developed to take that factor into account in terms of impact.

Dr. Miranda mentioned that not everyone decides to pursue an academic career, and so it is actually acceptable for younger investigators to go into industry if that becomes their chosen career path. People doing so do not constitute failures in terms of the biomedical workforce. Dr. Birnbaum agreed, and observed that millennials often take a different approach, changing jobs much more frequently.

Dr. Manautou asked whether there is an idea of the proportion of MDs versus PhDs leaving research and whether it is a larger exodus of MDs driving this initiative. Dr. Birnbaum said the answer in total is unclear, but that the number of physician/scientists is certainly way down. Also, only about 20% of NIH-trained people end up being PIs in academia, she observed. Dr. Ahsan said that that could be due to a number of reasons beyond not getting NIH grants. Dr. Birnbaum noted that the effort to lower the age of investigators is mandated by the 21st Century Cures Act. Dr. Collman said she was unaware of any systematic studies of people who have lost their grants to determine their next steps or their ultimate career decisions, and suggested that would be a good direction for research.

IX. Adjournment

Dr. Birnbaum thanked the presenters, the Council members, and the staff for their participation in the meeting. She said it was great to hear about so many exciting NIEHS/NTP programs, and encouraged everyone to fill out the survey on the new Strategic Plan. Dr. Collman added her thanks to everyone.

The meeting was adjourned at 11:00 a.m., June 7, 2017.

CERTIFICATION:

/s/

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

/s/

Gwen W. Collman, PhD
Executive Secretary
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Attachment:
Council Roster