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

MINUTES OF THE ONE HUNDRED FORTY-FIFTH MEETING OF THE NATIONAL ADVISORY ENVIRONMENTAL HEALTH SCIENCES COUNCIL

June 2-3, 2015

The National Advisory Environmental Health Sciences Council convened the open session of its one hundred forty-fifth regular meeting on June 2, 2015 in the Rall Building, Rodbell Auditorium, National Institute of Environmental Health Sciences, Research Triangle Park, NC. The closed session of the meeting was held June 3, 2015.

The meeting was open to the public on June 2, 2015 from 8:30 a.m. to 5:00 p.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 3, 2015 from 8:30 a.m. to 11:30 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
Kelly Brix, MD (*ex officio*) (by telephone, June 2 only)
Philip Brown, PhD
Lisa Conti, DVM
David Eaton, PhD
Kevin Elliot, PhD
Kenneth Fasman, PhD
Andrew Feinberg, PhD
Tomás Guilarte, PhD
Howard Hu, MD (by telephone)
Ron Johnson, PhD (*ex officio*)
Norbert Kaminski, PhD
Randall Kramer, PhD
Linda McCauley, PhD, RN
Marie Lynn Miranda, PhD
Edward Postlethwait, PhD
Viola Waghiyi

NIEHS Staff

Kathy Ahlmark
Janice Allen, Ph.D.
Robin Arnette, Ph.D.
Joellen Austin
John Balbus, M.D.
Martha Barnes
Linda Bass, Ph.D.
Linda Birnbaum, Ph.D.
Helena Bonner
John Bucher, Ph.D.
Danielle Carlin, Ph.D.
Lisa Chadwick, Ph.D.
Kelly Chandler, Ph.D.
Pamela Clark
Jennifer Collins
Joel Collinson
Gwen Collman, Ph.D.
Yuxia Cui, Ph.D.
Caroline Dilworth, Ph.D.
Christina Drew, Ph.D.
Lisa Edwards
Donald Ellis
Benny Encarnacion
Shannon Farris, Ph.D.
Michael Fessler, M.D.
Symma Finn, Ph.D.
Christine Flowers
Mary Gant
Barbara Gittleman
Alicia Graham
Kimberly Gray, Ph.D.
Janet Hall, M.D.
Shaun Halloran
Astrid Haugen
Michelle Heacock, Ph.D.
Heather Henry, Ph.D.
Jon Hollander, Ph.D.
Chip Hughes
Michael Humble, Ph.D.
Nina Jaitly, M.D.
Laurie Johnson
Evan Johnson
Bonnie Joubert, Ph.D.
Helena Kennedy
Annette Kirshner, Ph.D.

Alfonso Latoni, Ph.D.
Cindy Lawler, Ph.D.
Alicia Lawson
Kelly Lenox
Jennifer Martinez, Ph.D.
J. Patrick Mastin, Ph.D.
Kim McAllister, Ph.D.
Steven McCaw
Roseanne McGee
Liz McNair
Kirsten Mease
Aubrey Miller, M.D., M.P.H.
Sri Nadadur, Ph.D.
Sheila Newton, Ph.D.
Aaron Nicholas
Liam O'Fallon
Mitsue Parrish
Kristi Pettibone, Ph.D.
Jerry Phelps
Nicole Popovich
Molly Puente
Elizabeth Ruben
Angie Sanders
Dale Sandler, Ph.D.
John Schelp
Thad Schug, Ph.D.
Daniel Shaughnessy, Ph.D.
Bill Schrader, Ph.D.
Carol Shreffler, Ph.D.
William A. Suk, Ph.D., M.P.H.
Kimberly Thigpen Tart, J.D.
Claudia Thompson, Ph.D.
Sally Tilotta, Ph.D.
George Tucker
Michelle Victolino
Chris Weis, Ph.D.
Allen Wilcox, M.D., Ph.D.
James Williams
Leroy Worth, Ph.D.
Rick Woychik, Ph.D.
Darryl Zeldin, M.D.

Members of the Public Present

Megan Avakian, MDB, Inc.

Christina Bear
Eric Bear
Philip Bourne, Ph.D., NIH (via videoconference)
Alicia Brown
Ernie Hood, Bridport Services, LLC
Mike Phillips, RTI International
Ivan Rusyn, Ph.D., Texas A&M University
Fikri Yucel, SSS

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 members Drs. Cheung, Conry and Wynn were unable to attend. She said that Dr. Ron Johnson was attending in Dr. Wynn's stead. Drs. Hu and Brix attended by telephone. She asked all present in the room to introduce themselves, which they did. She asked the Council members attending by telephone 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 the voting process.

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 February 2015 Meeting Minutes

Approval of the February 2015 minutes was moved and seconded, and Council voted unanimously to approve the minutes. 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 2015 Council meeting.

In her Legislative Report, she described several recent Congressional hearings on NIH funding, and mentioned that the House and Senate have passed a budget resolution for FY 2016. The resolution raised concerns that there could be flat or decreasing budgets over the next 10 years. If there is no budget bill passed, sequestration would return in

2016, and would be "more painful" than the 2013 cuts. She described recent legislative briefings that she had delivered, as well as recent developments in Toxic Substances Control Act (TSCA) reform initiatives. She also updated the panel on the 21st Century Cures Act and the Secret Science Reform Act of 2014, which has passed the House but which President Obama has pledged to veto. The Cures Act represents "a glimmer of hope" for NIH, she said, as it would provide to NIH $10 billion dollars over 5 years outside of normal appropriations. She added that the bill has "a fairly good chance" of being passed, and would be "a lifesaver for NIH" if sequestration returned.

Dr. Birnbaum thanked NIEHS Legislative Liaison Mary Gant for her 27 years of service, as she is retiring at the end of July, and led all meeting attendees in a warm round of applause.

Turning to science advances, she briefly summarized several recent publications by NIEHS/NTP personnel or grantees. She began with two studies involving several NIEHS divisions, epitomizing the "One NIEHS" concept. She continued with short summaries of recently published studies from DIR, DNTP, and DERT researchers.

Dr. Birnbaum related several recent items of NIEHS news and highlights, including several examples of translation and outreach activities. She also cited several examples of current initiatives related to data and technology, and provided an update on recent NTP programs. She mentioned several recent meetings and events of note, including an IOM Roundtable on environmental exposures and obesity, an International Symposium on Alternatives Assessment, and the March 2015 SOT meeting, which saw considerable participation by NIEHS. She highlighted several upcoming meetings relevant to the NIEHS mission.

Dr. Birnbaum noted the recent addition of Jennifer Martinez, Ph.D., to head the Inflammation and Autoimmunity Group, and Shaun Halloran, the new Operations Manager for EHP.

She recognized many recent awards and recognitions gained by NIEHS staff and grantees, including NIH Director's Awards to NIEHS participants in the NIH Epigenomics Roadmap Program, the NIH Microphysiological Systems Program Team, and the Sexual and Gender Minority Research Coordinating Committee. Dr. Samuel Wilson also received the Ruth L. Kirchstein Mentoring Award, an NIH Director's Award.

V. Report of the Director, DERT

Dr. Collman reported to the council on recent activities and developments within DERT.

She initially set the themes for the Council meeting, much of which would be devoted to data, in the form of big data, data science, collaborations, and data sharing, along with

attention to resource needs for environmental epidemiology studies. She tied the data theme to Goal 7 of the NIEHS Strategic Plan regarding the use of knowledge management techniques, and described several data science efforts across NIEHS, including a timeline of NIEHS data sharing efforts. She mentioned several steps NIEHS is taking to implement recommendations from the 2011 Data Sharing RFI and the 2012 Data Sharing Workshop.

In the epidemiology community, many data science challenges remain to be addressed, she said.

One method of addressing those needs is a new vehicle to facilitate collaborations around data sharing in the EHS research community, an online tool called the Epidemiology Resources Catalog, which is modeled on similar data science efforts at NHLBI, NCI and NINDS. The catalog lists the cohort, case-control, and cross-sectional studies funded by DERT. It is designed to encourage new collaborations and data sharing in the EHS community, as well as to maximize NIEHS investments and to provide junior investigators a path to initiate ancillary studies. It will be rolled out in three phases: a searchable table (the tables are available online now at http://www.niehs.nih.gov/research/supported/cohort/index.cfm, although they're not searchable yet), to be followed by individual detail pages for each grant, and eventually improved search and filter functions. Potential long-term steps may include an EHS Epidemiology Consortium and an integrated data repository. DERT intends to work with its principal investigators to further develop and refine the tool going forward.

Dr. Collman noted that DERT embraces the role of data science and is initiating a dialogue with investigators in its landmark program areas.

Regarding the catalog, Dr. Fasman suggested that prior to attempting to establish an integrated data repository DERT should consider adding the capability for the website to act as a broker or intermediary for data requests to the principal investigators, including tracking whether data access was granted or denied. Dr. Collman agreed that that would be a good idea for tracking purposes. Dr. Fasman said he felt that NIEHS was "relatively poor at funding the long-term life cycle of access to data from older studies," and wanted to know how NIEHS might address that issue in the context of the larger data science and sharing discussion. Dr. Collman agreed that NIEHS has been handling longer-term data issues using traditional approaches, largely leaving it up to the investigator to determine how to manage long-term data, and so often the issue has been neglected. With changing times and evolving utility of the data, she said, the process must be reconsidered, with new mechanisms identified in the context of how money for the portfolio is apportioned. She acknowledged that a new approach is necessary, which would be enhanced and informed by Council's suggestions and ideas, as well as the steps taken by other NIH ICs to address the issues.

Dr. Eaton noted that there would be issues surrounding data sets that have an impact on a regulatory process, in terms of outside, non-NIH-funded parties interested in accessing particular data sets. He asked Dr. Collman how she would see managing that process. She said that it is not a new issue, and that it is to be anticipated that with a more transparent, open approach to data, such requests would probably increase. She said that the data cannot simply be put into the public domain due to unique challenges related to confidentiality. She said that NIH does not have a distinct policy on how to limit or broaden access, and that NIEHS is not intending to put data sets out directly to the public with the new online tool. A strategy has not been developed around providing access to data sets that are owned by universities, she noted. She said that an active dialogue would be necessary to delineate all of the associated issues and work to address them fairly. However, she added that it is important as a Federal agency to explore ways to promote maximal use of data NIEHS has invested in. She said it would be important to bring various members of the community together to explore how to deal with requests from outside parties, which involve tremendous use of time and resources to respond to.

Dr. Miranda noted that there is no mechanism in the application or annual report process to ensure that people are structuring or documenting their data sets in meaningful, appropriate, state-of-the-art ways, which makes data sharing difficult. She recommended that some standardization of reporting data be established and required of all grantees. She added that NIEHS needs to determine a better way to engage statisticians and informaticians, not just epidemiologists. Dr. Collman replied that those issues are part of the conversation around landmark programs—big programs solicited by RFA. She said that moving forward there can be special requirements around these issues in those programs. She noted that some of the steps would involve retrofitting existing programs to upgrade and standardize management systems, and that the new elements of data management should be part of the requirements for new studies.

Dr. Ahsan approved of the initiatives Dr. Collman had presented, particularly as they would help junior investigators gain access to data. He asked what the plan might be to integrate data resources from other sources. Dr. Collman replied that the conversation around that issue is just beginning, and that the community is being engaged in developing the necessary new standards.

Dr. Brown said he would like to see a feedback, report-back mechanism integrated into the catalog. Dr. Collman agreed that would be a worthwhile addition.

VI. NIH as a Digital Experience

Philip Bourne, Ph.D., the NIH Associate Director for Data Science, presented "NIH as a Digital Experience" to the council via videoconference from Bethesda. In his talk, he

outlined the broad trends affecting data science at NIH, including the spectrum from digitization to democratization. He said that currently biomedical science is at the point of deception along that spectrum, having just passed the initial point of digitization of basic and clinical research and electronic health records. Ultimately, the process will lead to true patient-centered health care. He cited the Precision Medicine Initiative as one major leap forward in the evolution, as it will be comprised of a national research cohort.

He shared that his group, the Office of Biomedical Data Science, intends "to use data science to foster an open digital ecosystem that will accelerate efficient, cost-effective biomedical research to enhance health, lengthen life, and reduce illness and disability." He detailed four overall goals by 2020:

- Enable major scientific discover through the BD2K initiative
- Establish and provide evidence of a more sustainable, efficient and productive data science ecosystem, both internal and external to NIH
- Establish and provide evidence of a well-trained and diverse workforce able to use and develop biomedical data science tools and methods
- Build upon NIH's leadership and reputation in data science

He described and provided detailed plans for five actionable areas to achieve those goals: sustainability, workforce development and diversity, discovery and innovation, policy and process, and leadership.

One of NIH's major data infrastructure initiatives is a conceptual framework known as The Commons, consisting of digital objects, search capabilities, and computing platforms such as public cloud-based platforms, super-computing platforms, and other platforms such as in-house computing solutions and private clouds. The Commons is currently being tested in pilot studies.

Dr. Kaminski asked Dr. Bourne about his concept of encouraging citations of shared or integrated data; whether it would come from publications or would extend beyond that, and how the issue of data quality would be dealt with. Dr. Bourne acknowledged that Dr. Kaminski had raised a critical point, with several pieces involved. He said that often data in publications is judged by the results of the study, not by actually looking at the data itself. He stressed that the data needs to be readily accessible. He said that the current situation of having data buried in journal sites for supplemental information is not useful, making it often very hard to find. He added that data quality is "clearly paramount." He said that a data discovery index could include crowdsourced quality information.

Dr. McCauley asked Dr. Bourne about the trajectory involved with electronic health records and other large scientific databases. He said that there is much energy coming from the Precision Medicine Initiative, which is drawing more attention to the electronic health records as a cohort. He said that currently they are a stumbling block in terms of interoperability and accessibility, but that the trend is moving in the right direction. He noted that the involvement of private sector entities would help, but that NIH has not done well with that, and that his group is trying to determine how to improve that situation.

Dr. Eaton said that at his institution, the University of Washington, a Master's of Science Program in Data Science is being built, in recognition of the importance of the field as no longer just a support role, allowing the opportunity for data scientists to be full-fledged faculty members. He asked Dr. Bourne if a master's degree is enough, whether there may be training grants available, and his general impression of the training needs for data science. Dr. Bourne said he had been around since the beginning of bioinformatics, and that he sees a parallel development with what is happening now with data science. He felt that a master's would be a good way to start the process, helping to establish the field as a legitimate scholarly endeavor.

Dr. Elliott asked Dr. Bourne what he thought were the most important aspects of training for team science related to data science. Dr. Bourne said that his group at NIH is spending 20% of its budget on training, but there is not a focus on collaboration per se. Cultural change for environments where data is shared should embrace and promote team science, he added.

Dr. Fasman asked what the biomedical research community might be able to learn from other scientific communities that have been driven down the path earlier and faster, for example, the high-energy physics community. Dr. Bourne agreed that there is much that can be learned from those communities. He noted that they often aggregate around the use of large instruments, and so are different from the biomedical community in how they operate. He said they have a much more collaborative environment driven by shared data sets—a completely different culture than in the life sciences. He added that there is a need for NIH and the biomedical science community to embrace people from that orientation much more than has been the case previously, including people from other domains such as astronomy and high-energy physics.

VII. Data Science Discussion

Dr. Cindy Lawler introduced and then moderated a discussion period designed to elicit ideas and suggestions from Council members on how the institute should move forward on a variety of data science fronts.

She observed that data science is closely connected to the 4 Vs of big data: volume (the increase in the sheer amount of data), velocity (the rapid rate of data production), variety (the coming together of various types and sources of data), and veracity (data quality). Databases, visualization, statistics and machine learning are other parts of data science, she added.

She noted that the goal of the discussion would not be to define data science more clearly, but to take a broad view and start the conversation and to identify next steps. As a starting point, she provided a list of DERT data science highlights, including active involvement in the BD2K program. Seeking to understand the data science challenges in environmental health sciences, DERT has also engaged the extramural community in various ways in recent years, with RFIs and workshops related to data sharing and to development of a framework for EHS language.

Dr. Lawler gave several examples of DERT data science-related work, including the Comparative Toxicogenomics Database and CHEAR, the Children's Health Analysis Resource, among others.

The key overarching question for Council members to consider, she said, is where does NIEHS belong in the data science landscape?

The open discussion began with remarks from assigned Council discussants Drs. Feinberg, Fasman, and Miranda.

Dr. Feinberg: "This is a train that's obviously left the station, and we want to be part of it, but it's important to focus on the issues that matter in terms of environmental health in particular." He focused on two elements: the integration of orthogonal data sources that include exposure, which is difficult and challenging, and issues regarding data security. Where do you keep these large data sets and how do you analyze them? They should be robust enough to be useful to both the generating groups and to outside investigators. He described a project he is currently involved in which is studying two identical twins—one of whom is currently living in space and the other is on Earth. He said the samples being delivered are being studied for a wide variety of metrics—an "incredibly robust group of measurements." How to deal with so much and such varied data is quite a challenge, he said. He noted that the astronauts are concerned about their privacy, where their data may jeopardize their flight status. He said that overall, focusing on the environmental issues in particular would help gain understanding.

Dr. Fasman noted that Dr. Birnbaum and Dr. Collman had asked him to represent the NAEHSC as part of the multi-Council working group for Dr. Bourne's office, advising on extramural grants related to the BD2K initiative. For the past nine months, he has taken what he has learned in the past from Council and NIEHS leadership to guide his advice to Dr. Bourne's program. He asked whether his Council colleagues felt that that level of

communication is sufficient, or whether there should be a more active channel and more frequent discussion and dialogue.

Dr. Miranda commented that of the four Vs described by Dr. Lawler, NIEHS should focus on variety. She noted that "data science" is not the same thing as "Big Data," and that there is much more to modern data sciences than how big the datasets are. Thus, she said, NIEHS has a comparative advantage in focusing on the variety element. In order to do that, a culture change will be required at the Institute and among its investigators, as well as the broad community of people associated with NIEHS through funding or other reasons. Training on data sciences, especially for new investigators, should be supported and made a priority. She recommended incorporating requirements in applications regarding architecting and data documentation. She also observed that there should be more of an effort to make NIEHS more appealing to statisticians and informaticians. Also, reviewer mindsets need to change to accommodate modern data science techniques and approaches.

Dr. Brown said that currently bioinformatics people are not given full consideration for promotions, tenure, and other professional considerations. Dr. Miranda felt that Dr. Brown's point was related to the current replicability problem and wondered why good data collection, quality assurance and architecting is not more highly valued.

Dr. Feinberg asked where grant reviews take place, internally or at CSR. Dr. Lawler replied that they take place at both.

Dr. Collman asked for feedback regarding data science needs in landmark programs. Dr. Miranda suggested a requirement for grantees to submit their metadata files. Thus, data would not have to be released prior to analysis.

Dr. Eaton suggested that NIEHS and/or NIH offer supplements for graduate education on big data. It would allow existing, funded programs to be involved from the ground up in training data specialists, with co-mentoring by a laboratory scientist and a bioinformaticist or statistician. It would also help train the next generation of scientists.

Dr. Lawler asked the panelists to describe training programs in this area.

Dr. Feinberg said that it is hard to get interdisciplinary training programs funded, especially those that cut across institutional boundaries such as schools. He added that more experienced people need to serve on review panels. Dr. Collman noted that in the larger funded programs, there is an opportunity to take control of how data is utilized, organized, and managed, and that currently there is no such requirement per se. Once such requirements are in place, the programs can be reviewed to ensure that the responses are of the highest quality during the peer review process. Dr. Feinberg emphasized the need for experienced people who have overseen interdisciplinary

programs to serve on peer review panels. Dr. Birnbaum noted that a subcommittee of the Science Management Review Board is currently studying those issues as they relate to peer review, and that recommendations should be forthcoming soon.

Dr. Miranda wondered about the follow-up to data sharing plan requirements in large grants. She endorsed the idea to include inquiries regarding data sharing in annual reports. She noted that getting people to share their data is actually quite difficult in practice, and that a requirement for public reporting might make it easier. She recommended linking data sharing plans with metadata. Dr. Collman said that data sharing plans are reviewed at the time of award, with follow-up on a case-by-case basis by program personnel. There is no comprehensive set of policies guiding the process, she added. Dr. Miranda said it sounded like the program officers were being relied upon to recognize failure to honor data sharing commitments, as opposed to requiring the investigators to demonstrate that they are honoring those commitments. Dr. Birnbaum noted that the 21st Century Cures Bill currently being considered by Congress includes a legal requirement for data sharing.

Dr. Feinberg said that some investment at the NIH level would be required, with some sort of mechanism to disseminate information rapidly to the community as a whole. He said that dbGaP is dysfunctional, with access being very difficult. He felt that it would be important to think completely differently about the culture of collectively disseminating information.

Returning to Dr. Collman's question about landmark programs, Dr. Fasman asked how things would change in the community if the default position in those programs would be for the applicants to describe how the data associated with the project would be made fully publically available, as a starting point. The endpoint would always be full public availability. "I'd like to see the community take a very aggressive stand," he said, "pushing people to that full publication point, and then asking them to define and justify the hurdles and the interim points in between." Dr. Collman asked the panelists to respond to that idea.

Dr. McCauley said there was a thin line involved with the public availability of data, with an assumption that data can be combined in some meaningful way. She noted that some of the parties who would like to have access to data are not necessarily friends. "This is hugely complex, with many different levels of concern and structure and purpose that we need to think about," she observed. She wondered if NIEHS should have a minimal dataset that would be included on the front end of projects to allow for combination approaches.

Dr. Miranda said she was not sure she was comfortable with full public availability of data, with protection of human subjects considerations in mind. She felt that perhaps

platforms with approved IRB protocols would be more appropriate. Regarding Dr. McCauley's point about combination of data, she said that a good data scientist may have creative ways of doing so. Dr. Brown added that there may be opportunities for focused RFAs associated with those creative data combination approaches. Best practices could be determined to help applicants avoid having to formulate data monitoring plans from scratch.

Dr. Feinberg felt that Dr. Fasman's concept of having complete open sharing as a starting point did not necessarily preclude protection of human subjects.

Dr. Miranda asked whether NIH can hold prize competitions. Dr. Birnbaum noted that there is a new one related to climate change being launched, and that others have been conducted in the past. Dr. Miranda thought it might be a good way to attract young people to contribute in the data science area.

Dr. Collman asked the Council members leading the discussion to move the discussion into toxicology or other animal data. She noted that there had been a lukewarm reception in the community to the idea of adding data to the CEBS database, and was curious why that might be the case. Dr. Conti asked whether Dr. Collman had any feedback about why there was the seeming resistance. Dr. Collman said that some had responded that it was easier for them to work on the data themselves. Dr. Fasman compared the situation to the history of GenBank, which started as voluntary in terms of data submission and then moved to such submission becoming mandatory. As people were required to add their data, the community began to put pressure on those who ran GenBank to make it more useful. He suggested that perhaps some number of people who were reluctant to put their data into CEBS were concerned about its design or utility. He said that if people are forced to put their data into it, with funding to enhance the database with analytical and visualization tools, there would be a "wonderful virtual cycle" generated, but the key is to make it mandatory. Dr. Eaton agreed, observing that as for CEBS, people did not know what was in it for them.

Dr. Postlethwait wondered how the uniformity of data fit into the larger questions, and how it could be accomplished. Dr. Miranda said that uniform data is ideal, but not necessary. She noted that sometimes data sets considered to be uniform are not actually, and that even when that is discovered, it does not mean the data are not usable. She described the influence of uncertainty, which highlights the need for expert statisticians. Dr. Postlethwait described his concept of uniformity in more detail, including the challenges involved with attempts to normalize data. Dr. Fasman said that "we don't wrestle with those questions and we don't resolve those questions as long as we're satisfied that we keep our data in our individual labs." As soon as there is community agreement that data will be pooled, he noted, then the tough work is done by hammering out a compromise, with belief in the value of the collective. He cited the

example of how gene expression data were collected 20 years ago, but when the value of collectivity was seen, standards and rules were determined, which have stood the test of repeated changes in technology. He suggested that the Institute could fund the work that is necessary to establish standards in toxicological data. Dr. Miranda agreed, but noted that the simple step of requiring people to publish their metadata would be interesting both programmatically and for data scientists to study in terms of discerning potential collective learning.

Dr. Feinberg discussed a potential "GIGO" problem—Garbage In, Garbage Out. He said the field should be very careful about that, and that data standards should be rigorous.

Dr. Woychik read an email from Dr. Allen Dearry, who was following the discussion remotely. He mentioned that there were currently 5 RFAs under the BD2K training opportunities. Dr. Eaton said they were actually very different from what he was proposing, as formalized training grants. His idea, he reiterated, was adding supplements to existing research grants.

Dr. Birnbaum closed the data science discussion, noting that it is a huge issue, not only affecting the extramural program, but throughout the EHS field. She said "if you build it they will come," in that by putting out the data, people will start using it. However, she acknowledged that there are extra issues involved with environmental data, but that those are not insoluble problems.

VIII. Epidemiology: Contributing to basic science by looking at the big picture

NIEHS Science Director Dr. Darryl Zeldin introduced Dr. Allen Wilcox from the Epidemiology Branch for the meeting's scientific presentation.

Dr. Wilcox said that epidemiology is usually thought of as the scientific arm of public health. The macro-level observations of epidemiology can also provide insights or raise fundamental hypotheses of interest to laboratory scientists. Some examples come from NIEHS epidemiologic studies of fertility and pregnancy. The number of fertile days in a typical human menstrual cycle—long underestimated by biologists—was resolved in an epidemiologic study. Another example from epidemiology is the discovery of a connection between the rate of development of a fertilized human egg and the rate of fetal maturation. Finally, new data show a connection between a mother's age and gene methylation in her newborn—suggesting the possibility of undiscovered mechanisms of methylation.

IX. Infrastructure and Methodological Research Support for Environmental Epidemiology Cohorts Concept Clearance

Dr. Kimberly Gray from the Population Health Branch presented the concept to Council for its consideration.

She included background information on the context of the concept. NIEHS supported 58 environmental epidemiology studies in FY 2013 and 2014 alone. In those years, NIEHS funded 47 large (≥250 subjects) environmental epidemiology cohorts (EEC).

NIEHS is proposing the creation of a mechanism to provide support for the maintenance of environmental epidemiology cohorts and their associated biorepositories and for the collection or development of additional measures in existing cohorts. The goal of the mechanism is to support the retention of trained personnel, ongoing longitudinal data collection, follow-up among study participants, and preserved integrity and quality of specimen collect that could otherwise be lost with breaks in funding. The mechanism will reduce the depreciation of invested resources and enable a greater continuity of research in the field. It is modeled upon a similar program in place at NCI.

The mechanism is to address two broad categories: cohort maintenance and methodological research. Cohort maintenance functions include participant engagement and follow-up, systematic assessment of biological markers to interpret or validate new research findings, data quality assurance and control, and data management and sharing. Support of methodological research involves development of novel statistical methods, validation of exposures and health outcomes, and biorepository organization and management.

The concept allows for the fragmented infrastructure components of an EEC to be consolidated under a single award and allow continued funding of the NIEHS investment in established EECs. An R24 or U24 funding mechanism is proposed. The program will be solicited through a broadly focused PAR or RFA, with a single annual receipt date for three consecutive years. Individual projects are capped at $350,000 direct costs with a maximum of 7 years of support, with the possibility of competitive renewal. It is anticipated that 2–3 awards will be made annually.

Dr. McCauley was the first Council discussant. She said she was very excited about the program. "I think this is something that has been needed for a long time," she commented. She likened the concept to maintaining a primate colony, in that it similarly maintains a very important colony of human research subjects, as well as maintaining quality in laboratories, ensuring that studies will continue and be replicable. She said she could not see a downside to the proposal.

Dr. Miranda was the second Council discussant. She fully supported the cohort maintenance aspect of the concept, but expressed some concern about the methodological research element. She worried that the combinations of people who are the right combinations to do cohort maintenance may not be the right combinations of people to do the methods development. She was concerned that the opportunity to achieve synergy with what NIEHS might be able to accomplish in data sciences might be lost if the two elements are coupled together. She suggested that it might be possible to pull the two elements apart, with two separate competitions. That would allow data scientists from anywhere to weigh in and propose to work on data from the cohort maintenance element. She felt that would create the right incentives for new collaborations, allowing new and exciting science to evolve.

Dr. McCauley said it was her impression that an applicant did not necessarily need to address both elements. Dr. Gray asked whether the mechanism should operate as a drop-down box, with the applicant picking which element to address. Dr. Miranda said that as proposed, applicants would be required to have cohorts, precluding the possibility of independent informaticians or data scientists without cohorts to apply. That would miss the opportunity to leverage the program to advance the Institute's interest in data sciences, she added.

Dr. Hu was the third Council discussant. He said that these cohorts stoke the creativity of researchers to go far beyond their original hypotheses, often generating significant exposure biomarkers. He noted that when budget cuts come to centers, the first thing to go is often infrastructure, as the original hypothesis-driven science must be protected. All cohort investigators struggle with infrastructure-related issues, he observed. He wondered if NIEHS itself could serve to provide shared best practices and coordination functions. He acknowledged that there is often a reluctance to fund infrastructure, but most of the cohorts have "really well measured environmental exposures." He suggested adding a piece to the program to which all investigators in the field could contribute, to help drive forward exposomics.

Dr. Feinberg detailed several of his concerns, despite the fact that he supports the idea of having a streamlined mechanism for cohort preservation. Having read through the concept document, he wished to put forth several cautionary notes. First, a cohort resource should not continue to be supported if it has not led to good, productive research. Second, it must have a special, unique quality that distinguishes it from others. Third, it is important that materials were collected under standards that persist for further research that might be done. Fourth, a program to be funded should fit within the Institute's strategic priorities. Fifth, there should be a management review associated with maintaining a cohort. Also, he recommended that cohort programs should be open for others to become involved, and he discouraged new statistical development associated with cohort maintenance.

Dr. Kramer asked for more information regarding the pros and cons of the U and R mechanisms. Dr. Gray explained how some of the other institutes are using such mechanisms in this area. Dr. Kramer asked if there was any preference between the two. Dr. Collman averred that the U mechanism might be most desirable for developing data resources and fitting in with NIEHS programmatic goals.

Dr. Kaminski said he agreed with the points presented by Dr. Feinberg. He said he could certainly understand using these kinds of funds to maintain valuable cohorts, but that could also see how the funding mechanism could end up being used as simply a supplement to existing programs, presenting an opportunity for misuse.

Dr. Birnbaum said that the idea of having the funding be a cooperative agreement as opposed to an individual grant would work against the concerns raised by Drs. Kaminski and Feinberg. She noted that it will be a new mechanism for NIEHS and would take some trial and error going forward. She pointed out that as the program might expand through the years, it could take away funding from R01s. However, she said she personally thinks it is a necessary step to help maintain the investment in significant cohorts.

Dr. Miranda said she agreed with the concept of maintaining good cohorts, but wished to emphasize that the two questions of cohort maintenance and methods development are separable. Dr. Birnbaum agreed that that is an interesting idea worthy of more consideration by NIEHS.

Dr. Brown endorsed the concept, and noted that it may be a way to bring non-EHS people into the EHS fold. He said the data management and data science need to be very clearly integrated into the program.

Dr. Postlethwait asked how knowledge of the 7-year cohort maintenance funding might impact review of new population study applications where establishment of new cohorts is proposed. Dr. Collman said that long-term cohort funding is the desire of all epidemiologists, so that long-term questions can be asked and answered. She noted that this proposal was not to serve for all applications in population science, but is designed to fill identified gaps.

Dr. Guilarte asked how the R01 portfolio might be affected. Dr. Collman said more financial modeling will be necessary before the RFA is prepared, and it is not just a simple equation as to how it might affect the full portfolio payline, since it changes the types of grants being offered. It would not simply cannibalize one program to fund another. Dr. Birnbaum said that in addition to the Strategic Plan goals Dr. Gray mentioned, the program would also support Goal 10, the economization goal.

Dr. Collman said that DERT staff will consider and incorporate these comments from Council as we continue to develop the program.

Dr. Kaminski asked if Council would have another opportunity to review the program once changes have been made resulting from its input. Dr. Collman said that would not take place, given Council's broad go-ahead. She pointed out that if the details of the RFA were brought to Council for approval, members would not be able to apply.

Dr. Collman called for a motion and second to approve the concept. Council voted unanimously in favor.

X. A World of Collaboration: Update on the NIEHS Global Environmental Health Program

Dr. John Balbus, Senior Advisor for Public Health and Director of the NIEHS-WHO Collaborating Centre (WHO-CC) for Environmental Health, updated Council on NIEHS Global Environmental Health (GEH) activities.

He correlated NIEHS GEH activities with the NIEHS Strategic Plan, pointing out that it was recognized as one of the plan's overarching themes. He traced the history of GEH as a formal program at NIEHS, stemming from 2008. He described the facets of the NIEHS GEH program, which is comprised of a GEH Working Group with 32 members across the Institute, a GEH Steering Committee with representatives of the four major NIEHS divisions, and the WHO-CC, with eight Focus Area Leads. The GEH program connects research to translation across NIEHS, he said.

Dr. Balbus started by summarizing NIEHS's extramural research in global environmental health, noting that from FY 2012–2014, there were 157 active GEH projects at sites around the world. Metals were the most-studied exposures, and neurological/cognitive disorders were the most-studied health outcomes.

He then turned to the activities of the NIEHS GEH program, and he outlined steady growth in the volume and success of communications/outreach activities, including substantial growth in GEH website views per year since 2012, a thriving newsletter with viewers from 177 countries, and 12 podcasts now available for listening. Also, since tracking started in 2013, GEH personnel have participated in 13 peer-reviewed publications and have made presentations at 22 meetings.

Dr. Balbus described the 6 areas of focus for the NIEHS WHO Collaborating Centre: climate change, children's health, electronic waste, cookstoves and household air pollution, the WHO Chemical Risk Assessment Network, and developmental origins of health and disease.

His major themes were:

- NIEHS maintains a diverse portfolio of global environmental health research and training funded projects.
- The GEH program has expanded NIEHS outreach and visibility on global environmental health.
- The WHO-CC provides a platform and a lens to focus scientific activities on topics of greatest global health importance.

Dr. Kramer said there appears to be good progress toward the GEH goal in the NIEHS Strategic Plan. Given how underfunded the WHO is, he inquired whether most of the funding for the GEH activities was coming from NIEHS. Dr. Balbus stated that the funding NIEHS provides to the GEH program, primarily funds NIEHS activities. He said that NIEHS is contributing to the capacity of the WHO-CC by bringing its capacity in, but does not directly alleviate its problem of short budget. Dr. Kramer asked if WHO is bringing anything to the table in terms of resources for the collaboration. Dr. Balbus said they do have staff working on various programs, and that it is a true collaboration, but there is no transfer of funds in either direction.

Dr. Feinberg said he was confused about the program's purpose, scope, and mission. Relative to the number of projects, he felt that the publication record was lacking. He wondered if the program was mainly an educational and networking tool. If so, he asked what the metrics would be. Dr. Balbus returned to his organizational slide, and noted that the publication metric he cited was only derived from the small, modestly funded group in the Director's office. He said the number of publications deriving from GEH research projects would be much greater. Dr. Feinberg speculated that perhaps the science itself was not put forth in the presentation, causing his confusion. Dr. Birnbaum noted that GEH is a One NIEHS program, but is not a research program in and of itself, being more of a coordinating effort and a communications effort.

Dr. Guilarte said that the program is a wonderful opportunity to engage resources, including from the extramural community. Dr. Balbus said that part of what is done in the collaborations is to identify grantees relevant to the topic at hand, in order to connect grantees to relevant events and activities.

XI. Update on the Undergraduate Research Education Program (UP) to Enhance Diversity in the Environmental Health Sciences (R25)

Dr. Michael Humble, from the Genes, Environment and Health Branch, updated Council on the NIEHS UP programs, which align with Goal 9 of the NIEHS Strategic Plan. They provide support for junior- and senior-level undergraduates from the diversity categories to gain supervised laboratory, epidemiologic, statistical or other research experiences in the environmental health sciences. The undergraduates can be supported for 40

hours/week during the summer and up to 15 hours/week during the academic year, for up to two years. The programs need to demonstrate an association with a strong research and graduate program in EHS as evidenced by the presence of a funded NIEHS T32 training program, a strong base of funded EHS research, or a graduate program with a focus on EHS research training.

There is a budget of up to $100,000 in direct costs annually, for five-year awards. NIEHS has made 6 awards as of April 1, 2015. Dr. Humble described each of the six institutions and the PIs involved.

Awards included funds for the PIs to attend the NIEHS Training Directors Meetings. Re-release of the RFA in 2–3 years to expand the program is being considered.

Dr. Postlethwait asked what the success metrics would be to renew the program. Dr. Humble replied that due to the young age of the participating students it will take a while to see how successful the programs will be, but one measure will be whether the recipients end up pursuing EHS or similar careers.

Dr. Guilarte said it is a very important program, citing the need to build a pipeline of diverse students to enter EHS. He said his institution had received one of the awards, and had a full cadre of 8 students eager to start.

Dr. Feinberg asked how the program would be assessed for renewal in 2–3 years if it would be difficult to evaluate its results even after the current five-year award, as Dr. Humble had described. He asked what interim or surrogate metric of success could be used in the meantime. Dr. Humble replied that an interim measure would be how many students are actually finishing the program. He felt that even within 2–3 years, they should be able to see what the initial applicants' plans for the future might be.

Dr. Birnbaum said that the program is another good example of outreach programs like Scholars Connect to get students into labs and into mentoring, contributing to increasing diversity in the biomedical workforce. She said that despite much commitment to that goal over the last 20–30 years, the effort has been "spectacularly unsuccessful," and that it is to be hoped that new programs such as UP will improve outcomes.

Dr. Brown said that his institution is engaged in mentoring at all levels, including postdocs and graduate students, and he would encourage others with T32 grants to include undergraduates as well.

XII. Adjournment

Dr. Birnbaum thanked all of the Council members and staff for their participation in the meeting.

XIII. Consideration of Grant Applications

This portion of the meeting (8:30 a.m. – 11:30 a.m., June 3, 2015) was closed to the public 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).

XIV. Adjournment

The meeting was officially adjourned at 11:30 a.m., June 3, 2015.

CERTIFICATION:

/s/

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

/s/

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

Attachment:
Council Roster