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

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

September 9-10, 2015

The National Advisory Environmental Health Sciences Council convened the open session of its one hundred forty-sixth regular meeting on September 9-10, 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 September 10, 2015.

The meeting was open to the public on September 9, 2015 from 8:30 a.m. to 4:30 p.m., and on September 10, 2015 from 8:30 a.m. to 10:15 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 September 10, 2015 from 10:15 a.m. to 12:00 p.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
Vivian Cheung, M.D.
Jeanne Conry, MD, PhD
Lisa Conti, DVM
David Eaton, PhD
Kevin Elliot, PhD
Gary Ellison, PhD, NCI (by telephone)
Brenda Eskenazi, PhD
Kenneth Fasman, PhD
Andrew Feinberg, PhD
Tomás Guilarte, PhD
Howard Hu, MD (by telephone)
James Johnson, Jr., PhD (*ex officio*)
Norbert Kaminski, PhD
Randall Kramer, PhD

Linda McCauley, PhD, RN
Donna Mendrick, PhD (*ex officio*)
Edward Postlethwait, PhD
Viola Waghiyi (by telephone)

NIEHS Staff

Kathy Ahlmark
Janice Allen, PhD
Bruce Androphy, JD
Joellen Austin
Michael Baker
David Balshaw, PhD
Martha Barnes
Linda Bass, PhD
Linda Birnbaum, PhD
Rebecca Boyles
John Bucher, PhD
Danielle Carlin, PhD
Lisa Chadwick, PhD (by telephone, Sept. 10)
Pamela Clark
Jennifer Collins
Tammy Collins, PhD
Gwen Collman, PhD
Justin Crane
Yuxia Cui, PhD
Sally Darney, PhD
Francesco DeMayo, PhD
Caroline Dilworth, PhD
Christina Drew, PhD
Lisa Edwards
Benny Encarnacion
Symma Finn, PhD
Kimberly Gray, PhD
Virginia Guidry
Janet Hall, MD
Astrid Haugen
Michelle Heacock, PhD
Jerry Heindel, PhD
Heather Henry, PhD
Jon Hollander, PhD
Joseph Hughes
Michael Humble, PhD
Laurie Johnson
Evan Johnson
Bonnie Joubert, PhD
Helena Kennedy

Annette Kirshner, PhD
Alfonso Latoni, PhD
Cindy Lawler, PhD
Alicia Lawson
Xiaoling Li, PhD
Robin Mackar
J. Patrick Mastin, PhD
Kim McAllister, PhD
Steven McCaw
Roseanne McGee
Liz McNair
Kirsten Mease
Sheila Newton, PhD
Liam O'Fallon
Kristi Pettibone, PhD
Jerry Phelps
Nicole Popovich
Tina Powell
Molly Puente
Les Reinlib, PhD
Elizabeth Ruben
John Schelp
Thad Schug, PhD
Daniel Shaughnessy, PhD
Natalie Shaw, MD
Bill Schrader, PhD
Carol Shreffler, PhD
William A. Suk, PhD, MPH
Kimberly Thigpen Tart, JD
Claudia Thompson, PhD
Sally Tilotta, PhD
George Tucker
Fred Tyson, PhD
Paul Wade, PhD
Nigel Walker, PhD
Leroy Worth, PhD
Rick Woychik, PhD
Demia Wright

Other (non-NIEHS) Staff
Lawrence Tabak, DDS, PhD, NIH (by telephone)
Carrie Wolinetz, PhD, NIH (by telephone)

Members of the Public Present

Megan Avakian, MDB, Inc.

Daniel Baden, PhD, UNC-Wilmington
Michael Baker, MDB, Inc.
Elaine Collier, MD, NIH
Ernie Hood, Bridport Services, LLC
John Ludlow, PhD
Mike 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 Drs. Miranda and Wynn were unable to attend. She said that Dr. Gary Ellison was attending by telephone in Dr. Winn's stead. Drs. Hu and Waghiyi 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 May 2015 Meeting Minutes

Approval of the May 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 May 2015 Council meeting.

In her Legislative Report, she discussed the budget situation, indicating that there was still the possibility of a government shutdown. She reviewed the proposed appropriations for NIEHS, NIH, the Common Fund, Superfund, and the NIEHS/DOE Training pass-through. She described the current status of appropriations in the various Congressional committees. She went over the progress of research-relevant legislation, including the 21st Century Cures Act, which has passed the House, with a similar bill under development in the Senate. She discussed the status of Toxic

Substances Control Act (TSCA) reform legislation, with different bills under consideration in the House and Senate.

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

She went over several examples of NIEHS news and highlights, including the establishment of new core centers at North Carolina State University and the University of California, Davis. Staff updates included the hiring of Sally Perrault Darney, PhD, as the new editor-in-chief at *Environmental Health Perspectives* and Franco DeMayo, PhD, as Deputy Chief of the Reproductive and Developmental Biology Laboratory. She also noted several new developments in training. She mentioned several recent meetings and events of note, relating each one to the applicable goals in the 2012-2017 NIEHS Strategic Plan. She described several upcoming meetings relevant to the NIEHS mission.

She reviewed the recent awards and recognitions presented to many NIEHS staff members and grantees.

She described the full year of events coming in 2016 associated with the 50th anniversary of NIEHS, and reminded council members to send in their nominations for NIEHS history and research highlights to the website devoted to that purpose.

Dr. Eaton said he was struck by Dr. Birnbaum's comment on the Science, Teachers, and Research Summer (STaRS) program. He recalled that NIEHS had funded a program 30 years ago that provided a similar program to the extramural community. He said that some years later the rules changed and core centers could no longer count the program as part of their Community Outreach and Engagement Cores (COEC) activities. He felt that that should be revisited. Dr. Birnbaum agreed.

V. Update on the Common Rule NPRM

Dr. Carrie Wolinetz, NIH Associate Director for Science Policy, briefed the council by telephone on the Notice of Proposed Rulemaking (NPRM) issued by NIH, which updates regulations related to the protection of human subjects, known as the Common Rule, which was originally implemented in 1991. The modernization effort is designed to enhance safeguards and respect for research participants, while increasing the efficiency of the oversight process. It institutes several major reforms, including simplification of consent documents and streamlined IRB review, while also expanding the scope of clinical trials subject to Federal regulation. Among other provisions, it mandates that institutions in the US engaged in multi-site research must rely upon

approval by a single IRB, if appropriate. The provisions will take effect one year after publication of the final rule, with compliance mandated within three years of publication. As of September 8, 2015, a 90-day comment period was in effect. Public comments will be considered, the final rule will be developed, and ultimately the final rule will be published.

Dr. Eaton asked who would make a determination of exemption at a large research institution. Dr. Wolinetz replied that consistency of the process is the most important element. She said there would be some flexibility allowed in who would make that determination. Dr. Eaton asked if, for example, a school of medicine could make that determination without needing to go through its IRB. Dr. Wolinetz said she believed that would be allowed under the proposal.

Dr. McCauley asked for more information about the broad consent form Dr. Wolinetz had mentioned, as the rule allows broad consent for collection and use of biospecimens and identifiable data. Dr. Wolinetz said that that form is still under development, and will eventually be available for public comment.

Dr. Birnbaum thanked Dr. Wolinetz for her presentation, and said that she saw the NPRM as “an important move forward in the protection of human subjects as well as the facilitation of research.” She stressed to the council that this is an opportunity to read the NPRM, consider its provisions, and provide comments and suggestions to NIH.

VI. Developing the NIH-wide Strategic Plan

Dr. Lawrence Tabak, the NIH Principal Deputy Director, briefed the council by telephone on activities related to the development of the new NIH-wide Strategic Plan, which is designed to help guide the agency in fulfilling its mission over the next five years. He described the draft framework being discussed, which identifies three areas of opportunity that apply across biomedicine: fundamental science, health promotion and disease prevention, and treatments and cures. He noted that the unifying principles involved are setting priorities and enhancing stewardship. His report to the NAEHSC was just the second of 21 such presentations he will conduct through October, speaking to each one of the NIH ICs as part of the process of soliciting feedback. He said NIH was seeking broad suggestions, specific suggestions, and disease-specific comments, and has thus far received more than 1,000 comments. Once the plan is finalized, it is to be presented to Congress by mid-December, 2015. He invited Council members to submit their thoughts to him at his personal NIH email address.

Dr. Feinberg asked Dr. Tabak about integrative science as a strategic priority, with multidisciplinary research presenting new opportunities for collaborations across NIH institutes and with other agencies. He also commented about the importance of recognizing high-risk, high-reward research, especially the importance of programs that

reward exceptionally creative, talented people. He said he understood that NIH supported such programs with ½ to 5% of its budget. Dr. Tabak said that Dr. Feinberg had articulated some of the elements that are currently under intense discussion. He said that NIH recognizes the importance of multidisciplinary, multi-agency research, and is looking for ways to facilitate more of it, particularly as concerns review of applications for such research. He added that the interest in high-risk, high-reward research is spreading, and needs to be more pervasive throughout the ICs and beyond simply the Common Fund.

Dr. Eaton asked if the Strategic Plan addresses the opportunities for inter-agency collaboration and funding of research. He also endorsed Dr. Feinberg's comments about the importance of NIH investment in high-risk, high-reward research. Dr. Tabak replied that the plan will address the need for NIH to foster additional relationships, both with sister operating divisions within HHS and with other entities such as NSF, EPA, and others, as well as the private sector.

Dr. McCauley asked whether anyone had raised a concern about the burden of chronic disease in the US, and where that might fit under the three areas of opportunity in the plan. Dr. Tabak said that it has been brought up, and it transcends the areas of opportunity. He noted that another topic of discussion had been the idea of multi-disease trials, since patients typically present with more than one condition.

Dr. Hu noticed the attention to health disparities and population science in the plan, as well as big data. He said that with the advent of the Internet of Things and big data, there is an opportunity to incorporate other aspects of individuals' lives that contribute to disease burden, as well as their utilization of health systems. He suggested that NIH may want to consider partnering with other federal agencies such as DOT, the Department of Agriculture, and the Department of Labor, because they have access to data that can enrich understanding of determinants of health and preventable determinants of disease. Dr. Tabak agreed with Dr. Hu's comments, and recognized that relevant data sets may be found with non-traditional partners, in order to mine different dimensions of human experience.

Ms. Waghiyi related some of the health disparities plaguing her home area in Alaska, and asked Dr. Tabak to speak further about advances in elimination of health disparities. Dr. Tabak said that NIH-wide, those important issues need to be addressed. He said that in the era of big data, there are new opportunities to convert technological devices into sentinels, as personal, home, or even community-based monitors. He noted that all of NIH is responsible for reducing health disparities, with that effort featured in the strategic plan. Ms. Waghiyi emphasized the importance of involving affected and vulnerable communities in initiatives to combat health disparities. Dr.

Tabak agreed that involvement by research participants as full partners, at the individual, family, and community levels, is vital in research efforts.

VII. Report of the Director, DERT

Dr. Collman updated the council on activities and developments within DERT since the last meeting in June. She introduced Demia Wright, who has been hired to be a public health educator within the Worker Training Program. She was previously with the CDC.

Dr. Collman spent the balance of her presentation on reviewing FY 2015 DERT accomplishments as they relate to the 2012-2017 NIEHS Strategic Plan. She went through each of the 11 strategic goals encompassed by the plan, and gave specific examples of DERT accomplishments within each area. She further categorized each summary within the topics: Raising Awareness, Building Collaborations, and Advancing Research; Moving the Science Forward: Programs and Initiatives; and Building the Knowledge Base: Publications and Other Products.

Dr. Collman praised her team, whom she said do great work in many different areas.

Dr. Birnbaum observed that “we’re really living the strategic plan, and I think it’s making a huge difference in what we do.” Dr. Fasman added that he has been involved in many strategic planning exercises over the years, and has “never seen an organization embrace the process and embrace the implementation” so thoroughly. He said the institute should be commended for how it is living the process, to the advantage of environmental health science. He said it is particularly exciting to see the progress in areas that were under-addressed when the plan was originally formulated. He asked Dr. Collman about Goal #7, Using knowledge management techniques, in terms of coordinating activities. Dr. Collman replied that there have been some coordinating activities, including efforts to establish interoperability among the programs. She said there is an effort to build standardized approaches in the data center activities. Dr. Fasman asked if follow-on RFAs to specifically encourage the community to use those pooled resources were being considered. Dr. Collman said there would be, in the future.

Dr. Brown said he was pleased with the attention to citizen science, and asked how it would be considered in light of the NIEHS/DERT portfolio. He noted that such efforts bring in many people from outside the environmental health arena. Dr. Collman said it would be important to learn more about the efforts to help inform how the institute should respond. Part of the discussion, she said, is to inquire about what the community needs, envisioning how it might appear in five years. She said that NIEHS has practiced citizen science before, under different rubrics. She noted that the consideration is internal at this point, and that when they feel the time is right, it will be brought to Council.

Dr. Kramer said he was particularly interested in Goal #10, and how discussions have gone on about incorporating economic analysis. He asked if it was anticipated that there would be funding opportunities in that area. Dr. Collman said it was under consideration, along with issues of environmental policy and environmental health policy. She said there are currently 8 grants incorporating economic analysis, with other such evaluations being considered. When it is an area deemed suitable for further investment, it would be brought to Council for more feedback.

Dr. Eskenazi said she was "astounded by the breadth and depth of what DERT does." She asked about Strategic Plan Goal #9, particularly in terms of increasing diversity in the environmental health sciences. She felt that starting the process at the undergraduate level is too late, and wondered if pushing it back into the high school level had been considered, potentially as a way to help disadvantaged students get into college. Dr. Collman said that the institute did have some programs that reach out to younger students. From a grant mechanism approach, she added, it gets more complicated the younger you go. She said some funding in a research line was being used to help identify promising people at the undergraduate level by giving them research internship opportunities over the last two years of college. Given the limited dollars available, the focus is on the college-age pipeline, she added.

VIII. Environmental Health Sciences Core Centers (EHSCC) Evaluation Discussion

Dr. Christie Drew provided a brief introduction to the session. She said that work on the EHS Core Centers evaluation began more than two years ago. One year ago, the evaluation subcommittee comprised of four Council members and three outside experts, began its proceedings. It was asked to assess the ability of the Core Centers program to produce complex, translational, and emerging environmental health research.

Dr. Linda McCauley, Council member, who chaired the evaluation subcommittee, presented its findings and recommendations to the Council. She provided background information about the program, the required components of EHS CCs, and the centers that participated in the evaluation. She described previous evaluations from 2004 and 2010. The current evaluation collected both process and outcome data. She described the timeline and work steps involved in the evaluation process and went over the summative evaluation questions the subcommittee had pursued. She briefly discussed each of the six key findings and four recommendations contained in the subcommittee's final report.

Six of the seven evaluation advisory subcommittee members gathered in a panel discussion setting to engage in a conversation with the Council about their work and report. The Council was represented by Dr. McCauley, Dr. Brown, Dr. Fasman, and Dr. Kaminski. They were joined by Dr. Dan Baden from UNC-Wilmington, and Dr. Elaine

Collier from NCATS/NIH. (Dr. Kari Nadeau, the seventh member of the subcommittee, participated by phone.)

Dr. Postlethwait said that the term "translation" needs a precise definition. He asked whether the subcommittee was planning to address that issue. Dr. Baden agreed that there are many, many definitions of "translation," not only in science but also in the business community. He said that his definition is that translational research results in a product, a process, a data set, or something of value. He noted that Congress has been asking NIH what it gets as a return on its investment, and said that translational research is one way to answer that question. The definition needs to be operationalized for grants, centers, and the public. Dr. Kaminski agreed that clearly the research needs to make some kind of practical impact. He felt that the definition of translational research should be kept broad, so as not to stifle creativity. Dr. Collier said that it is a matter of taking basic discoveries and translating them into something that impacts health. Dr. Birnbaum asked if the subcommittee had looked at the "cloud" diagram from the NIEHS Strategic Plan, which provides an idea of how NIEHS sees translation. Dr. Kaminski said they had looked at the cloud diagram, and talked quite a bit about it. He likened translation to taking the basic science observations and trying to apply them to practical outcomes. Dr. Postlethwait suggested keeping it simple, to come up with some other verbiage describing translational research, concentrating on the concept of "translating" research. Dr. McCauley said that is a key concept, but great care must be taken with language in this instance. She said it is apparent that there are "real nuggets" of translational research, but it was difficult to include them in the report, because they weren't reported in that context.

Dr. Eaton said he had been involved in a CTSA effort at the University of Washington, and his group had spent "innumerable hours debating this exact question." He said they had come with a wheel diagram depicting the various steps of research. He suggested that it would be an understandable, sensible model that could be consulted, obviating the need to "reinvent the wheel." Dr. Baden said the subcommittee had looked at the cloud diagram, and said that part of the goal of coming up with a definition was to be able to look at translational research so that it could be repeated. Dr. Fasman said the group definitely was not "going back to square one," examining several of the existing definitions and diagrams. He noted that in EHS, the work is in populations with an emphasis on prevention and leading to policy, as opposed to the disease and patient-oriented emphasis in some other related fields. He said the group's goal was to express the EHS emphasis with respect to the existing models. Dr. Brown added that the concept is similar to "bench-to-bedside," but could be called "bench-to-creekside" in the case of EHS – very much the difference between clinical medicine and public health. Dr. Collier said the model is neither linear nor circular, but could go from basic to population, with many ways of getting things done. Clearly, she added, this

area of science does not fit the disease model. Dr. Brown noted that NIEHS has always been "extremely translational," in terms of practical use of scientific results to improve health, so this is working to define something that the institute already does quite well.

Dr. Eskenazi said that the two examples of translational work that Dr. McCauley had cited were actually interventions, and in order to be translational, evaluation must be built in, which costs money. If the recommendation is to include a better translational component, there should be dollar signs attached in order to properly evaluate. Dr. Collier acknowledged that metrics came up repeatedly in the group's deliberations.

Dr. Elliott said he had been impressed with the multi-directional communication among the COECs and the communities. He asked if in the assessment, the subcommittee had found good opportunities for the cores to learn from each other in terms of community involvement and communication. Dr. McCauley said the communication among the core centers, sharing best practices, was a positive factor. She added that the publications being put forth regarding community interface are bringing value to the entire scientific community. Dr. Baden described the "tremendous positive history" of the COEC cores, when there was much discussion about the definitions of community engagement and community participation. Dr. Brown added that the subcommittee had found interesting ways the COECs were integrated.

Dr. Kaminski said that Dr. Elliott had brought up some important questions and challenges that face both P30 and Superfund centers. He noted that the themes of many of the centers coalesce around the expertise at the grantee institution, and in the case of the P30s, often there is already a threshold of NIEHS funding that allows a center to be competitive. When a theme is determined, then the need is to find a population or community with whom to engage. Sometimes, that may involve traveling long distances to find the appropriate community. Dr. Collier said she felt that this was one area of extreme strength within the EHS community.

Ms. Waghiyi said that from the map Dr. McCauley had shown, it appeared that most of the centers in the evaluation were east of Texas. She asked how the institutes or regions had been selected. Dr. Birnbaum replied that they are selected on the basis of a peer review process, by evaluating who has the best science. She noted that two new centers were located at UC-Davis and North Carolina State University. She said that most of the large population centers in the country were represented, but that that did not mean that all of the desired populations were included presently.

Dr. Hu noted that all had acknowledged that NIEHS is unique, being more public health oriented. He said there is a space missing in the conversation, living between the scientists talking to the scientists and the scientists talking to the community outreach people and the community. When he moved to Canada, he said, it became clear that in

the US there is a disconnect between NIH and NIEHS and the federal and state public health agencies, which should be natural partnerships, but who seem to have differing agendas. He said there are products coming out of the centers that have great policy relevance for public health agencies, which would help bolster the impact of the NIEHS translational research agenda. He said that his group works quite closely with Public Health Ontario. Dr. Kaminski said that Dr. Hu had raised a very important point, and noted that the Superfund centers interact with local and regional government agencies. He said that there did not seem to be data on that issue from the P30s. Dr. Birnbaum agreed that it would be interesting to check with the core centers on their interactions with policymakers.

Dr. McCauley said it would be good to develop a framework to ask those questions as part of the metrics being collected, which could also encourage centers to conduct those interactions. Dr. Janet Hall, NIEHS Clinical Director, said that translational research seems to have evolved into something that has lost its original meaning. She noted that initially it involved thinking about "blocks" – why such amazing basic science research, or population research, were not getting to the next step and informing other areas. She suggested it might be useful to think about those blocks, particularly by center directors. She also noted that the Patient-Centered Outcomes Research Institute (PCORI) may offer lessons regarding community engagement. Regarding the "blocks" cited by Dr. Hall, Dr. Fasman said the subcommittee's idea was to fine-tune the existing model and determine which parts of it were under-represented, resulting in calls for focused funding and asking the centers to deal with those areas.

Wrestling with the issue of metrics, Dr. Brown said that at some point the subcommittee had turned to a qualitative, narrative approach and began to see that the stories people told about what their centers do gave much more information. He said there was a disjuncture between the actual metrics and members' knowledge of COEC work, for example. He said it might be interesting to look at one center quantitatively and another qualitatively, and then compare the two results. Dr. McCauley said she would like to see some opportunity for NIEHS to be able to demonstrate its expertise in patient-oriented approaches, such as with asthma populations, for example. Dr. Collier said it would be good to see environmental impacts being incorporated into the PCORI framework, so that the picture bigger than just medical interventions could be looked at.

Dr. Conry said that as an OB/GYN, she was faced with advising both patients and physicians. When asked why more science is not being translated, she said it was because the science is not well understood. She said the PCORI comes into play because it facilitates specific representations, for example in mercury or smoking cessation.

Dr. Conti said she was interested in the group's second recommendation about center directors and the sustainability of Center leadership. She asked if the subcommittee, in its review of earlier evaluations, found persistent problems that had not yet been addressed, or a thread running through the three evaluations. Dr. Kaminski clarified that the recommendation regarding center director succession came not because they thought any directors were not doing a good job, but more from the idea that the centers are hubs of intellectual interaction and mentoring, and so it is important to develop the junior scientists' leadership skills. Dr. McCauley added that the centers are complex, with multiple cores, community engagement, and career mentorship, for example, and those skills are not learned overnight. Dr. Baden said it would include what would happen in the event of the death of a center director. Dr. Conti asked if there was a need for a more formalized leadership institute. Dr. Baden said that there is an element of self-preservation in how a center handles leadership succession. Dr. Birnbaum said that her perception of the recommendation was that succession planning is needed, as with any other organization. Dr. Fasman noted the long history of the centers program, and stated that center existence or leadership should never been seen as an entitlement. Dr. Collier added that it is important to get the younger center members into situations where they can develop their leadership skills. Dr. Brown said that the core centers are different, in that their people are not dedicated to their own individual projects, but come together out of a shared interest. Thus, the director must herd people together in a way that may not be necessary at other types of centers, he added.

Dr. Collman noted from the group's report that NIEHS can also play a role in succession planning through involvement in annual meetings, looking to identify potential future leaders. Thus, the succession planning is a shared responsibility, she observed.

Dr. McCauley returned to Dr. Conti's second question regarding what had been learned from all three evaluations. She said it was a benefit to see that the subcommittee was not the first to undertake an evaluation. She said it was good that they had been asked to dig deep on what is complex, emerging, and translational research. She noted that the current process was very different from the two prior evaluations.

Dr. Hu said that an important element of the NIEHS and Superfund centers is that more than half of the predictive value of what will make a center application successful comes with the attention to detail, process, structure, and leadership – skills that are not taught in graduate school. He said he liked the concept of a leadership institute or workshop.

Dr. Postlethwait asked the subcommittee whether they had considered how the centers might facilitate the integration between population science and more mechanistic bench science. Dr. Kaminski replied that it is more an institute responsibility to do so, rather than the P30s. Dr. McCauley said that the centers must have a certain level of NIH funding, but their studies may not fit together in the way Dr. Postlethwait was describing.

However, she said, a wise center director will look for opportunities to link the two. Dr. Postlethwait said it appeared to be the inverse of the model employed by pharmaceutical companies.

Dr. Collier cited an example of a center that had developed an assay working with another center interested in the problem. Dr. Baden mentioned some other examples of cross-center cooperation. "The valuable part is that in these core centers there are enough people, some doing basic, some doing applied, some doing translational, some doing clinical or field, that you can put this all together," he said. He noted that the core centers had started as equipment cores, but have now grown into places of multiple capabilities.

Dr. Eaton said that many of the centers focus on that type of synergy between mechanistic and population work. He asked how the evaluators handled the challenge of assessing the core centers that have a lot of other NIEHS centers as part of the core center. Dr. Fasman noted that the subcommittee did not evaluate the individual centers, but had seen that where there was synergy, with multiple centers at an institution or collaborating centers across institutions, they were some of the more exciting efforts seen, and so part of the recommendation for improved metrics was to develop ways to measure those interactions. Dr. Eaton asked about situations where centers leverage NIEHS dollars with other NIH dollars. Dr. Brown said that did come up in the evaluation, and that some of the EHS achievements in the last fifty years have resulted from cross-institute collaborations. He suggested that it was time recalculate those associations, as a way to expand EHS to many more scientists outside of the immediate field.

Dr. Collier said it is also important that cores communicate so as to avoid duplication. Dr. Eaton noted that there is a downside to multiple funding, as it sets up a situation of dependence on both sources. Dr. Birnbaum said that it certainly does have a downside, but that collaboration and working together "has more ups than it does downs."

Dr. Birnbaum thanked the subcommittee and the Council for a valuable, productive discussion.

Dr. Claudia Thompson thanked the subcommittee for its hard work over the past year, and recognized the coordination work of Dr. Kristi Pettibone during the project.

IX. SBIR/STTR Grants at NIEHS in FY2015

Dr. Dan Shaughnessy updated the Council on the current status of the NIEHS SBIR/STTR program. He described the program, and shared some of its grant-making history. He said that in FY2015, 35 grants had been made so far, with a total of 38 expected by the close of the fiscal year. He delineated the types of unsolicited grants

that had been made, in exposure assessment tools, nanotoxicology, toxicology, biomarkers, the Superfund Research Program (SRP), and Education and Outreach. He provided examples of several of the programs that received support.

Dr. Heather Henry briefed the Council on SRP unsolicited SBIR grants, which support clean-up technologies and monitoring tools applicable to Superfund. She provided a list of grants, and described examples of companies that had received support.

Dr. Shaughnessy discussed solicited SBIR/STTR awards, which emerged from five RFAs. He described each of the RFAs and listed the awardees in each area. He discussed a new solicitation in FY2016: Phase IIB awards for validation and commercialization of approaches to reduce animal use in toxicology testing (U44), which will be a cooperative agreement. He discussed the program's strategies for increasing meritorious applications and outcomes by increased marketing and knowledge sharing. He noted the emerging high priority areas for the program, including tools for exposure, response to engineered nanomaterials, and tools for environmental health education, and asked for ideas for other new priority areas.

Dr. Fasman said he noticed in Dr. Shaughnessy's slide showing the current portfolio of funded projects, there was a higher percentage of nanomaterials proposals in Phase I, and relatively few in Phase II. He inquired whether that was because of newness of the program or a translation problem. Dr. Shaughnessy said he felt that it was due to a review problem. He noted that CSR now has a study section dedicated to nano biomaterials and nanotechnology, and so some of the applications may go there. He predicted that it would be an evolving process as people realize that it is an evolving technology need.

Dr. Kramer asked if there is an ability to track the eventual outcomes of the companies receiving grants. Dr. Shaughnessy described the current PODS tracking system, which tracks companies' sales, patents, and publications, although there is not an automated way to gather that information. He said the program is working diligently to develop such a system for evaluating return on investment.

Dr. Eaton asked for clarification about the "competing renewal" designation for the U44 grant for alternative methods. Dr. Shaughnessy confirmed that to qualify, a company must have already been funded under Phase II. He estimated that 12-20 companies would be eligible.

Regarding the solicitation of new emerging area ideas, Dr. Elliott suggested that new techniques to aid citizen science might be fruitful. Dr. Shaughnessy agreed that it would be useful to develop new sensors that would be more accurate but less expensive, making them appropriate for citizen science programs.

Dr. Collman noted that when she first came to DERT, the SBIR program was fledging, and said there had been an amazing evolution in the program since then in terms of outreach, focus, and targeted use of monies for technologies supporting environmental health.

X. SIRT1 in Metabolism, Tissue Homeostasis, and Human Diseases

Dr. Bill Schrader introduced the meeting's scientific speaker, Dr. Xiaoling Li from the Signal Transduction Laboratory in the NIEHS Division of Intramural Research.

According to Li, SIRT1 is a member of a family of proteins known as sirtuins, which regulate the body's metabolism and are believed to play a role in a number of cellular processes, such as metabolism, stress response, DNA repair, genome stability, and aging.

Her group's recent work has revealed critical functions of SIRT1 in embryonic stem cell biology, animal development, and cancer cell metabolism. The lab's studies are advancing understanding of the role of SIRT1 in mediating gene-environment interactions during development and disease, potentially providing the molecular basis for novel therapeutic targets related to a number of human diseases.

Dr. Mendrick asked Dr. Li to describe the types of environmental insults involved the process she had described. Dr. Li replied that certain chemical exposures had been identified as being associated with intestinal tissue damage.

Dr. Kaminski asked about the inflammatory response in the knockout mouse model, particularly in the gut. He wondered whether there was any evidence that bacteria or bacterial products were crossing the lumen, and what Dr. Li thought the trigger might be. She replied that the experiments suggested there might be a tissue integrity problem.

Dr. Eaton asked about other ligand-activated nuclear transcription factors, and whether SIRT1 might be involved in their regulation as well. Dr. Li said that her group had not looked into that, but that some microarray data they had seen suggested that it was.

Dr. Fasman noted that the biotech and pharmaceutical industries have shown much interest in sirtuins as drug targets. He asked if Dr. Li had followed the progress of early clinical trials in that area, and if she felt there was promise in that approach. She said that it is a controversial issue, and that she focuses her attention on the basic research, although she believes that SIRT1 may have promise as a therapeutic target.

Dr. Cheung asked about the targets of the antibodies in the process illustrated by Dr. Li. She replied that it is not currently known.

Dr. Postlethwait asked if Dr. Li had recolonized the mouse guts with lactobacillus, and if so, whether it had reversed any of the symptoms observed. Dr. Li said that that was currently being worked on.

Dr. Birnbaum asked if there was any evidence of polymorphisms in the SIRT1 genes in humans. Dr. Li said that SNPs had been seen in promoter region associated with SIRT1. Dr. Birnbaum noted that the global knockout model was embryo-lethal. She praised Dr. Li's efforts to conduct aging research in the area.

XI. PEPH Update

Liam O'Fallon provided the Council with an update on the Partnerships for Environmental Public Health (PEPH) program. He noted that PEPH had last been brought to the group seven years ago as a concept clearance.

He defined PEPH as an integrative program that breaks down programmatic silos to promote interactions among NIEHS grantees and community partners. Participants have shared interests in research approaches, communication methods, and evaluation methods, and focus on common themes such as health outcomes, populations, exposures, and partnerships. He described the goals of PEPH, and the many programmatic areas in which it is involved. He defined environmental public health, the framework of the program, as the science of conducting and translating research into action to address environmental exposures and health risks of concern to the public.

Mr. O'Fallon described many of the key accomplishments and benefits of the PEPH program since its inception in 2008. He illustrated how program development has been guided by the framework, as well as response to emerging needs. He provided several specific examples of PEPH programs, including an Evaluation Metrics Manual, the PEPH Resource Center, the PEPH monthly newsletter, and the group's podcast and webinar series, as well as other reports and network building activities. PEPH has also contributed to research, in program development and new EHS areas such as environmental health literacy and citizen science. PEPH launched the Research to Action program, which has brought together environmental and occupational health researchers with community members as a way to re-invigorate community-engaged research with a focus on research leading to public health action. He outlined plans for future programs and activities in communication and research, capacity building, and coordination and evaluation.

Dr. Conti said it was wonderful to see how the program has matured. She asked Mr. O'Fallon to discuss the inclusion of state environmental health directors, and how the state partners would be involved with future projects. He mentioned that it had been a while since he met with the state environmental health directors, but has recently been approached by the Association for Public Health Laboratories regarding the potential

role of state public health labs in citizen science and community-engagement efforts. He said that could be a good time to re-engage with state environmental health directors.

Dr. Eaton noted that although NIEHS is one of the smaller NIH institutes in budget, it is "a giant among the institutes in community outreach and engagement," thanks in no small part to Mr. O'Fallon's leadership.

Dr. Brown spoke in favor of continued increased support to PEPH. He related his history of involvement with the group. He said it would be important to be sure that program directors and grantees in all areas know more about PEPH and to encourage their involvement. He said that aside from its practical work, it has enabled a focus on conceptual activities.

Dr. Eskenazi speculated that one of the stakeholders who may be left out is industry. She wondered if in the next seven years PEPH might bring industry into the mix of outreach. Dr. Eaton agreed that that was an excellent idea, with some great opportunities.

Dr. Cheung suggested that there should also be inclusion of medical schools. Dr. Conry agreed with Dr. Cheung's suggestion, and said that as a clinical professional, she was unaware of PEPH previously. She felt that reaching out to medical schools, training programs, and medical societies would be an important step forward.

Dr. McCauley noted that over the course of the entire Council meeting so many pieces are interconnected. She said that PEPH is one great example of 15 years of significant NIEHS work. She suggested that NIH, in its current strategic planning effort, should look to PEPH as a model for community engagement and effective partnerships. Dr. Birnbaum reminded Council that Dr. Tabak provided his email address and invited such recommendations.

Dr. Elliott mentioned that he was helping to organize a conference at the University of Notre Dame in fall 2015 on citizen-industry collaboration. He asked about how some of the insights emerging from COECs and core centers might be passed on to other core centers. He asked how formally the PEPH links the core centers that are conducting outreach and engagement or outreach and translation. Mr. O'Fallon said that conferences and meetings are the face-to-face interactions, with webinars another channel. He said that the newsletter regularly features the efforts of a variety of community outreach and engagement cores. Also, in the future, the Resource Center would encourage people to identify their interests and areas of expertise, to foster cross-fertilization.

Dr. Fasman asked to what extent the core centers might be informed that a future metric of their success will be their engagement with PEPH programs. Mr. O'Fallon said that submitting materials to the Resource Center is already in the language of some RFAs. He said PEPH would prefer to emphasize the benefits of involvement, rather than requiring it.

XII. Concept Clearance: Environmental Influences on Placental Origins of Development (ePOD)

Dr. Thad Schug briefed the Council on a concept clearance on environmental influences on placental origins of development (ePOD). The overarching goal of the program is to determine how early life exposures affect placental health, and ultimately how the health of the placenta affects the health of the offspring and mother. The aims of the concept are to:

- Accelerate development and application of new models and methods for placental assessment
- Better understand the effects of exposures on early stage placental physiology, endocrine, immune, and metabolic functions
- Determine relationships between exposures, placental health, and subsequent effects on fetal and maternal health

Dr. Schug provided background information about the human placenta – an important but understudied organ with a variety of functions. He described the current NIEHS portfolio that includes placenta research; it contains just six grants. In its first phase, the proposed ePOD program would partner with NICHD and its Human Placenta Project. Phase two of ePOD would develop a cross-disciplinary, NIEHS-led program to better understand environmental influences on the placenta, including both human and basic research programs.

Dr. Conry was the first Council reviewer. She described her organization's involvement with placental research. She found the ePOD concept, particularly with its integration with NICHD, to be "an exciting opportunity to take what we don't know and the very large elements that we need to know, and put together a very important picture." She was particularly excited to hear about Phase Two of the project, with its focus on understanding both toxicants and teratogens. She said the project will be an opportunity to "jump ahead" in knowledge regarding the placenta.

Dr. Eskenazi was the second Council reviewer. She commended the concept, calling it "a no-brainer" and "essential." She said it was politically not possible to look at the first trimester, and at least part of the second trimester in the US in terms of placental development, which loses much understanding of placental development and its effect on fetal and maternal health. She added that the program should have set-aside

money, in that it is a new phase of research. She said that currently many researchers who have looked at the placenta have looked at it indirectly, but it would be preferable to be able to acquire tissue for direct study, and she hoped the RFA would encourage that. She said she was unclear about the distinction between the two phases of the program.

Dr. Schug replied that it is a rather broad concept, with the intent that it be an umbrella to cover several initiatives rolling out over time. The NICHD Human Placenta Project has been running for a year-and-a-half. There have been discussions about collaboration already, and NIEHS staff and grantees have been involved in meetings. Dr. Birnbaum added that with the 2015 National Children's Study funds, NICHD received $39 million to fund the Human Placenta Project over four years.

Dr. Feinberg said it sounded like a great concept. He said he was surprised that there were so few grants in the area. He suggested access and use of the material for epigenetic research. He said the placenta would be an appropriate tissue to consider, especially for prenatal exposure. He felt that the language in the concept proposal was tentative. He said, "We should just get the placentas. They're discarded." He said that cord blood and cord should also be included, and that there should be a real effort to acquire and bank those materials for research. He noted that it would fall well into the new consent (broad consent) idea from NIH. He asked for clarification about the federal guidelines regarding use of fetal material, and whether use of early pregnancy placentas would be allowed. Dr. Birnbaum said that of course those issues are much in the news currently. NIH has had to inform Congress about all of the studies that involve that type of material, she added. She speculated that the use of human embryo/fetal material would continue. She said that placenta is considered fetal material, and added that there are cultures where the placenta is not discarded.

Dr. Ahsan asked if the omics data from the Human Placenta Project would be publicly available. Dr. Schug said that it would be, under the Cooperative Agreement mechanism. Thus, Dr. Ahsan observed, NIEHS grantees would be able to integrate that information. He mentioned the theory that the placenta has a protective effect in the mother, preventing breast cancer. On that basis, he said he would hope that NCI would be involved as well.

Dr. Brown said he was very supportive of the project. He appreciated that Dr. Birnbaum had mentioned the cultural issues involved, and recommended inclusion of social scientists. He disagreed that collection of placentas would fall under broad consent, and felt that it would actually be narrow and continuing consent.

Dr. Kaminski noted that there seemed to be broad agreement that it is an important area. In terms of the omics data that can be generated, the technology is now so good

that incredible detail can be seen. He felt that there should be emphasis on the exposure side, so that the omics data could be linked to environmental factors. He hoped that the RFA would have a strong emphasis on measuring exposure. He asked whether cord blood would be considered to be part of the placental tissue, since it is such a rich source of stem cells. Dr. Schug said that the goal of the NICHD omics RFA is to look at early stage placentas from trimester one or two.

Dr. Feinberg felt that the concept should be broadened to include the other materials mentioned. Dr. Collman said that NICHD, in beginning the Human Placenta Project, had identified a gap in understanding of the very early time period, and identified imaging as one way to better characterize it. She said that the other materials raised by Council could be included in the NIEHS RFA, or NIEHS could go back to NICHD and discuss opportunities that might go beyond their current thinking. She said there are some materials such as cord blood available in repositories, so the opportunities and resources would be incorporated into the initiative. She said it would be useful to take Council's comments and see if NICHD would have an interest in broadening the scope of their program.

Dr. McCauley agreed that given the current public confusion over the use of fetal tissue, the timing of the proposal is not optimal. She said that NIEHS could perform a wonderful service by doing some health literacy around the issue, so that the public could better understand the relationship of environmental exposures and health. She hoped that the public's understanding could be moved, fighting some of the pushback that is not based on science. She said that access to health care facilities to acquire these samples is "hugely problematic." She said that biorepositories should be part of clinical care.

Dr. Conry said the problem is logistics. She said that at Kaiser Permanente, they have a large project to collect first visit blood from pregnant women. The investment in storing such materials for years is substantial. The collection is easy, but storage is difficult. She said that in terms of the public's misconceptions, "science doesn't matter," and that what is important is people's beliefs about the sources of tissue.

Ms. Waghiyi said that populations living in areas of military contamination and global pollutant contamination face not just harm to the fetus, but also threats to their way of life. She cited issues such as learning and developmental disabilities, birth defects, reproductive problems, and a crisis in cancer occurrence.

Dr. Collman said that Ms. Waghiyi's comments emphasized the importance of exposures in consideration of the placenta and pregnancy outcomes, as Dr. Kaminski had described. Dr. Birnbaum noted that this was a concept, and the discussion was designed to gather Council's ideas, and that it would inevitably change. She also

reminded Council that everything could not be done in one certain area, so the presentation was designed to present an initial framework for consideration. She noted that placentas are big and require much room for storage, which should be considered as efforts are funded.

Referring to Phase Two of the program, invoking the One Health concept, Dr. Conti said there is much to learn in this area from the veterinary perspective, including potential access to animal tissues.

Dr. Feinberg suggested that perhaps only 95% of placentas might be discarded, which might suffice for research purposes. Dr. Collman agreed that today researchers would think about how to save and store relevant parts of any tissue, using new sectioning methodologies. She emphasized that studying early stage placental tissue would yield different information from late stage, as they are actually different organs. Thus, research across the full nine months of placental development is needed.

Dr. Collman called for a motion to approve the concept. Dr. Feinberg so moved, and the motion was seconded. The Council members voted unanimously to approve the concept, including members on the telephone.

XIII. Consideration of Grant Applications

This portion of the meeting (10:15 a.m. – 12:00 p.m., September 10, 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/	/s/
Linda S. Birnbaum, PhD, DABT, ATS Chairperson National Advisory Environmental Health Sciences Council	Gwen W. Collman, PhD Executive Secretary National Advisory Environmental Health Sciences Council

Attachment:
Council Roster